Onco-Nephrology; a new concept

By

Mohammed Kamal Nassar

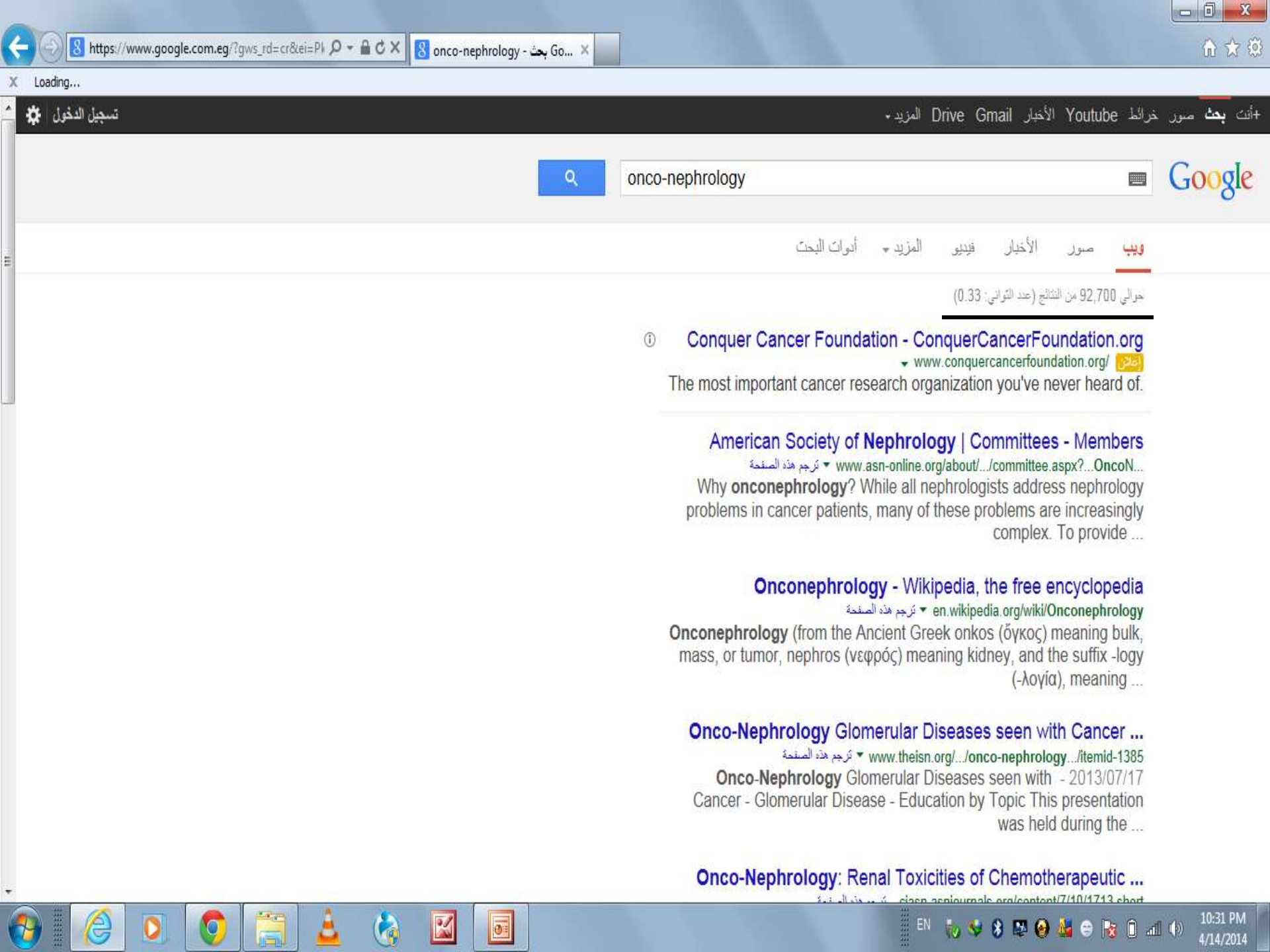
Assistant Lecturer of Nephrology

Mansoura University

Agenda

- Evolution of a subsubspeciality.
- Magnitude of the proplem.
- Cancer & CKD.
- Cancer & AKI.
- Kidney proplems in special oncological situations.
- To dialyse or not ???

Evolution of a subsubspeciality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onco-nephrology - بحث Go...
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onco-nephrology
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ويب صور الأخبار فيديو المزيد أدوات البحث
حوالي 92,700 من النتائج (عدد الثواني: 0.33)
Conquer Cancer Foundation - ConquerCancerFoundation.org
إعلان www.conquercancerfoundation.org/
The most important cancer research organization you've never heard of.
American Society of Nephrology | Committees - Members
ترجم هذه الصفحة www.asn-online.org/about/.../committee.aspx?...OncoN...
Why onconephrology? While all nephrologists address nephrology problems in cancer patients, many of these problems are increasingly complex. To provide ...
Onconephrology - Wikipedia, the free encyclopedia
ترجم هذه الصفحة en.wikipedia.org/wiki/Onconephrology
Onconephrology (from the Ancient Greek onkos (ὄγκος) meaning bulk, mass, or tumor, nephros (νεφρός) meaning kidney, and the suffix -logy (-λογία), meaning ...
Onco-Nephrology Glomerular Diseases seen with Cancer ...
ترجم هذه الصفحة www.theisn.org/.../onco-nephrology.../itemid-1385
Onco-Nephrology Glomerular Diseases seen with - 2013/07/17
Cancer - Glomerular Disease - Education by Topic This presentation was held during the ...
Onco-Nephrology: Renal Toxicities of Chemotherapeutic ...
EN
10:31 PM
4/14/2014

blood 2010 116: 3126-3127
doi:10.1182/blood-2010-08-299420

Transplant survivorship: a call to arms

Corey Cutler

In this issue of *Blood*, Sun and colleagues from the Bone Marrow Transplant Survivors Study report the chronic health outcomes of more than 1000 survivors of stem cell transplantation. Their results demonstrate a significant burden of chronic conditions among survivors.

AMERICAN SOCIETY OF NEPHROLOGY

Kidney Week 2011

PRELIMINARY PROGRAM

November 8 – 13

Philadelphia, Pennsylvania
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Registration and General Housing Opens June 1

ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

One-Day Early Programs
(Wednesday, November 9)

- Onco-Nephrology: What the Nephrologist Needs to Know about Cancer and the Kidney
- Polycystic Kidney Disease: Translating Mechanisms into Therapy

Moving Points
in Nephrology

Onco-Nephrology: What the Nephrologist Needs to Know about Cancer and the Kidney

Jeffrey S. Berns and Mitchell H. Rosner†*

Clin J Am Soc Nephrol 7: 1691–1691, 2012. doi: 10.2215/CJN.03240312

The field of oncology is rapidly changing as new therapies emerge and improve the outcomes for many types of cancer. Not surprisingly, the population with cancer, like the general population, is aging. As a result, patients with cancer are probably receiving diagnoses and treatment in the setting of more comorbid conditions, including CKD. Furthermore, there is an ever-growing list cancer, and those that result from cancer treatment. Dr. Perazella then comprehensively reviews nephrotoxicity of cancer chemotherapy, first explaining some of the reasons the kidneys are particularly susceptible to drug-induced injury, then addressing some of the most interesting renal complications of both newer biologic therapeutic agents and older, more classic, antineo-

*Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania; and †University of Virginia School of Medicine,

Moving Points
in Nephrology

Onco-Nephrology: AKI in the Cancer Patient

Albert Q. Lam and Benjamin D. Humphreys*†*

Summary

AKI is common in patients with cancer, and it causes interruptions in therapy and increased hospital length of stay, cost, and mortality. Although cancer patients are susceptible to all of the usual causes of AKI in patients without cancer, there are a number of AKI syndromes that occur more frequently or are unique to this patient population. AKI also confers substantially increased risk of short-term death, and the ability to reverse AKI portends a better outcome in some cancers, such as multiple myeloma. Several trends in oncology, including increased survival, better supportive care, older patients who have received multiple chemotherapy regimens, and new therapeutic options, are driving an increase in the numbers of cancer patients who develop AKI. As a result, nephrologists should be increasingly familiar with the diagnosis, management, and treatment of AKI in this setting. Here, we summarize recent data on epidemiology of AKI in cancer patients, describe the most common AKI syndromes in this population, and highlight emerging areas in the growing field of onconephrology.

Clin J Am Soc Nephrol 7: 1692–1700, 2012. doi: 10.2215/CJN.03140312

*Renal Division, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts; and †Lance Armstrong Foundation Adult Survivorship Clinic,

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Onco-Nephrology Forum

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- Mark A. Perazella, MD, FASN (2014)

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- Ala Abudayyeh, MD (2016)
- Joseph R. Angelo, II, MD (2014)
- Joseph V. Bonventre, MD, PhD, FASN (2014)
- Farhad R. Danesh, MD, FASN (2016)

- Why onconephrology? While all nephrologists address nephrology problems in cancer patients, many of these problems are increasingly complex. To provide the best nephrology care for cancer patient, we must understand rapidly changing protocols and therapies.

- Emerging kidney toxicities associated with drugs targeting VEGF and TKIs and other signaling pathways, tumor lysis syndrome, cytotoxic chemotherapy-induced kidney toxicities, kidney problems in myeloma, tumor or treatment-related microangiopathies and glomerulonephritis, stem cell transplant-associated acute and chronic kidney injuries, obstructive uropathies, severe fluid and electrolytes abnormalities, and dosing and timing of chemotherapy in CKD and ESRD patients: these and other complex problems, and their increasing frequency and severity, provide a unique and unprecedented opportunity for nephrologists to improve treatment for cancer patients worldwide.

- Onconephrologists help cancer care teams prevent kidney problems or resolve them as they arise, and improve patient outcomes. Research in cancer nephrology is already improving kidney care in cancer patients. A more focused approach to cancer nephrology may also help address challenges like renal cell carcinoma in end-stage renal disease.

MAGNITUDE OF THE PROBLEM

Table 1.10

Age Distribution (%) of Incidence Cases by Site, 2005-2009

All Races, Both Sexes

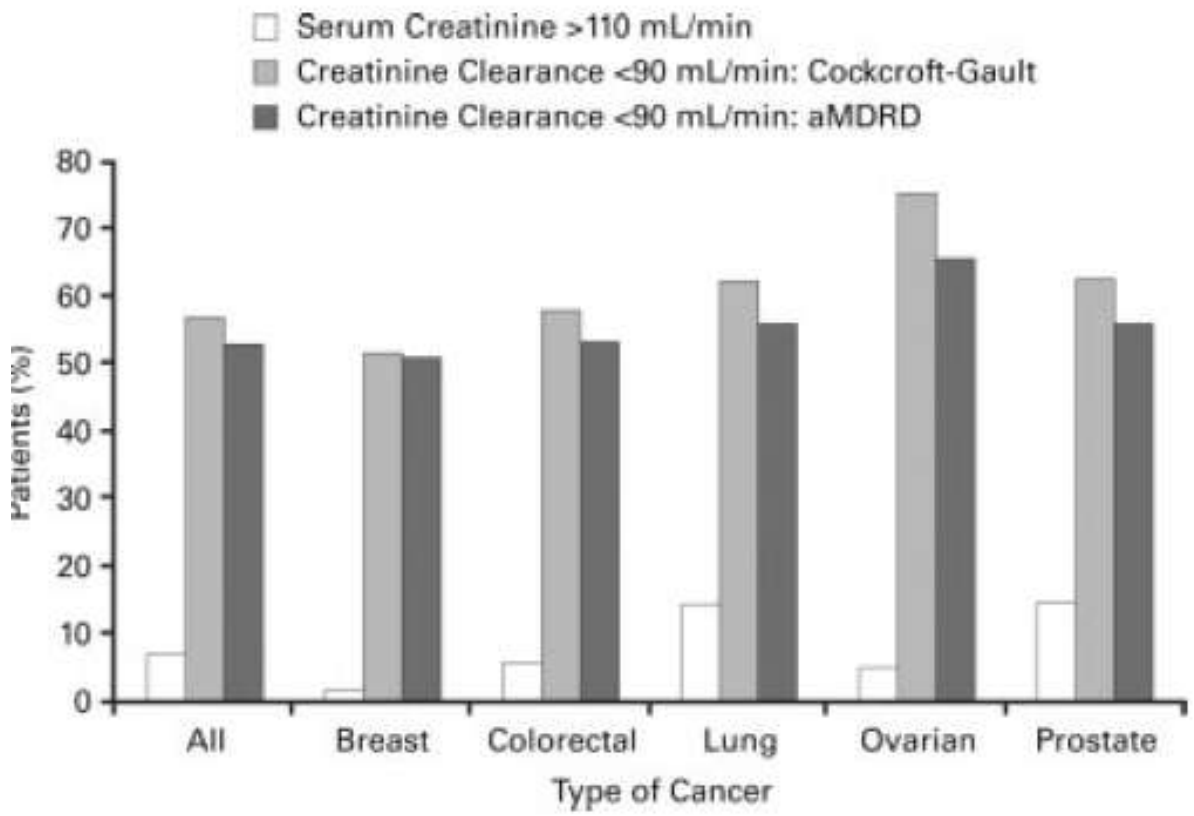
53.2%

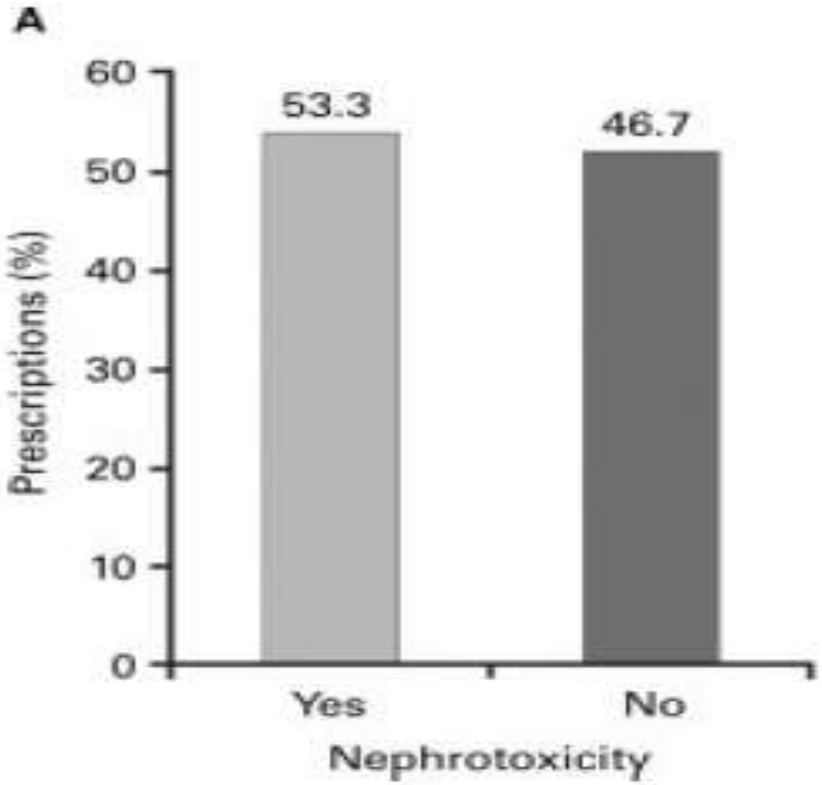
Site	Age at Diagnosis <20	20-34	35-44	45-54	55-64	65-74	75-84	85+	All Ages	Cases
All Sites	1.1	2.6	5.5	14.2	23.4	24.9	20.6	7.7	100.0%	1,922,239
Oral Cavity & Pharynx:	0.6	2.2	6.1	20.4	28.5	21.1	15.1	6.0	100.0%	45,554
Lip	0.1	1.1	5.6	14.7	18.1	22.5	24.8	12.9	100.0%	2,782
Tongue	0.1	1.9	5.8	20.6	32.1	21.9	13.0	4.6	100.0%	13,173
Salivary gland	2.1	6.6	7.6	14.5	19.2	19.2	20.6	10.2	100.0%	5,356
Floor of mouth	0.1	0.2	4.0	21.5	30.6	24.5	15.2	3.8	100.0%	2,497
Gum & other oral cavity	0.8	2.1	4.6	14.1	23.1	22.8	21.6	10.8	100.0%	6,259
Nasopharynx	3.5	5.7	14.3	25.1	24.1	15.7	8.9	2.7	100.0%	2,762
Tonsil	0.0	0.4	7.2	31.8	36.1	16.3	6.7	1.4	100.0%	7,450
Oropharynx	0.0	0.4	4.4	19.8	33.2	24.4	13.0	4.6	100.0%	1,619
Hypopharynx	0.0	0.1	1.8	16.9	31.1	27.9	18.1	4.1	100.0%	2,794
Other oral cavity & pharynx	0.2	0.7	2.4	15.3	29.6	26.3	18.3	7.1	100.0%	862
Digestive System:	0.2	1.0	3.7	13.3	21.6	24.3	24.6	11.3	100.0%	355,133
Esophagus	0.0	0.3	2.3	12.2	26.1	27.4	23.7	8.0	100.0%	18,572

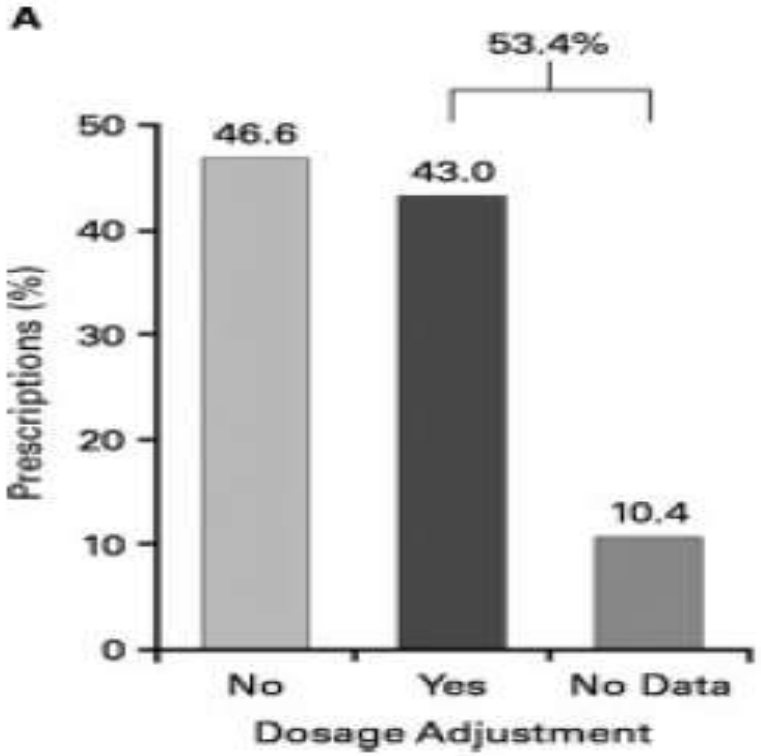
Prevalence of Renal Insufficiency in Cancer Patients and Implications for Anticancer Drug Management

The Renal Insufficiency and Anticancer Medications (IRMA) Study

DOI 10.1002/cncr.22904
Published online 17 July 2007 in Wiley InterScience (www.interscience.wiley.com).




A
60
50
40
30
20
10
0
Prescriptions (%)
53.3
46.7
Yes
No
Nephrotoxicity


A
53.4%
50
40
30
20
10
0
Prescriptions (%)
46.6
43.0
10.4
No
Yes
No Data
Dosage Adjustment

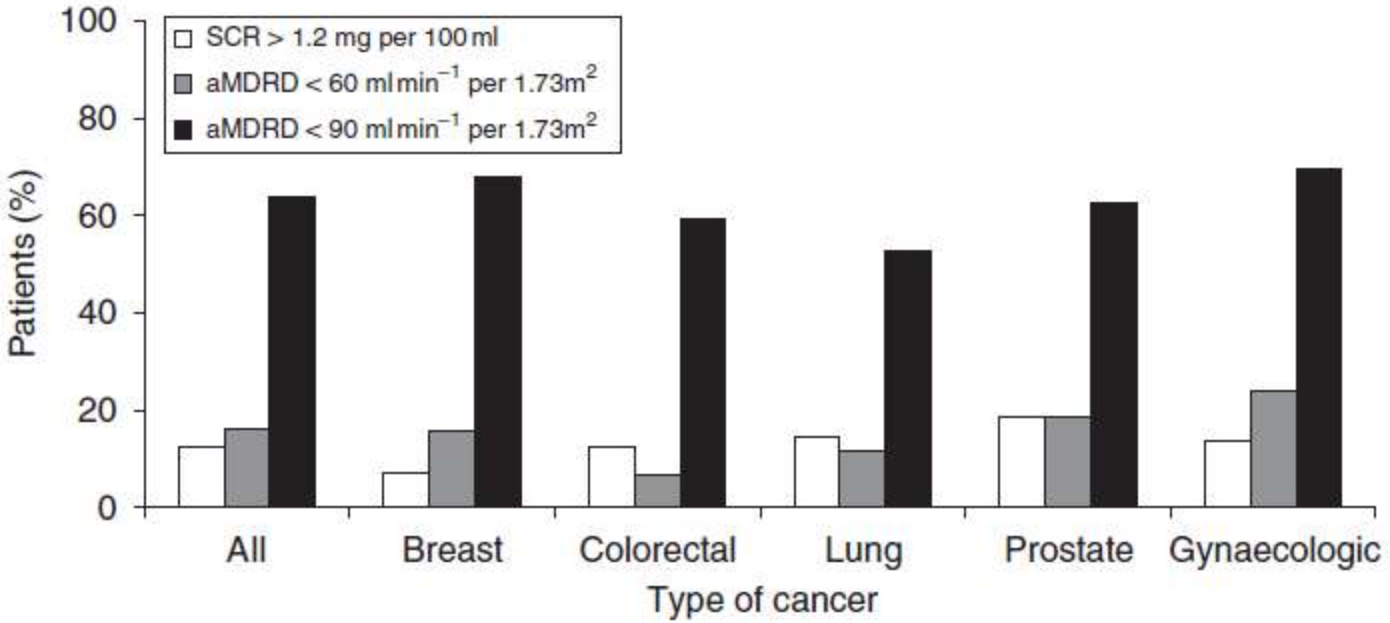
British Journal of Cancer (2010) 103, 1815 – 1821

www.bjcancer.com

Cancer and renal insufficiency results of the BIRMA study

N Janus*[,1], V Launay-vacher[1], E Byloos[2], J-P Machiels[3], L Duck[4], J Kerger[5], W Wynendaele[6], J-L Canon[7], W Lybaert[8], J Nortier[9], G Deray[1] and H Wildiers[2]

[1]Service ICAR, Department of Nephrology, Pitié-Salpêtrière Hospital, 47-83 Boulevard de l'Hôpital, Paris 75013, France; [2]Department of General Medical Oncology, Multidisciplinary Breast Centre, Leuven 3000, Belgium; [3]Department of Medical Oncology, UCL University Saint-Luc Clinics, Brussels 1200, Belgium; [4]Onco-Hematology Unit, Saint-Pierre Clinic, Ottignies 1340, Belgium; [5]Department of Medical Oncology, UCL University Clinics of Mont-Godinne, Yvoir 5530, Belgium; [6]Department of Medical Oncology, Imelda Hospital, Bonheiden 2820, Belgium; [7]Department of Medical Oncology, Notre Dame Clinic, Charleroi 6000, Belgium; [8]Department of Medical Oncology, AZ Nikolaas Hospital, Sint-Niklaas 9100, Belgium; [9]Department of Nephrology, Erasme Hospital, Brussels 1070, Belgium



Creatinine Clearance of the 4684 Renal Insufficiency and Anticancer Medications (IRMA) Study Patients According to Cockcroft-Gault and Abbreviated Modification of Diet in Renal Disease Formulae*

		CrCl							
	19.8%	Cockcroft-Gault formula				12% aMDRD formula			
Variable	All patients	<30 mL/min	30–59 mL/min	60–89 mL/min	≥90 mL/min	<30 mL/min	30–59 mL/min	60–89 mL/min	>90 mL/min
No. of patients	4684	61	864	1760	1513	43	518	1915	1766
%	100	1.3	18.5	37.6	32.3	0.92	11.1	40.9	37.7
Sex ratio (M:F)	0.55 (1667:3017)	0.9 (29:32)	0.46 (272:592)	0.56 (633:1127)	0.62 (579:934)	1.26 (24:19)	0.54 (182:336)	0.51 (649:1266)	0.61 (672:1094)
Age, y	58.1 ± 13.1	71.4 ± 11.7	67.2 ± 10.3	59.7 ± 11.1	50.5 ± 12.4	67.4 ± 12.3	65.4 ± 11.2	60 ± 11.8	53.9 ± 13.5
Weight, kg	65.8 ± 13.9	59 ± 15.5	58.4 ± 11	63.9 ± 11.8	72.7 ± 14.6	67.7 ± 15.3	67.4 ± 13.7	66.9 ± 14.1	64.3 ± 13.6
SCR, µmol/L	78.3 ± 35.4	248.3 ± 157.7	96.8 ± 27.1	76. ± 16	63.4 ± 14.1	312.2 ± 151	114.1 ± 22.6	80.3 ± 12	59.9 ± 10.8
CrCl, mL/min	83.3 ± 30.7	22.1 ± 6.8	49.2 ± 7.8	74.6 ± 8.5	115.4 ± 23.6	19.7 ± 7.4	50.7 ± 7.3	76.1 ± 8.2	113.6 ± 31.5

Creatinine Clearance of the 3903 Renal Insufficiency and Anticancer Medications (IRMA) Study Patients With Normal Serum Creatinine Levels According to Cockcroft-Gault and Abbreviated Modification of Diet in Renal Disease Formulae

16.6%

6.5%

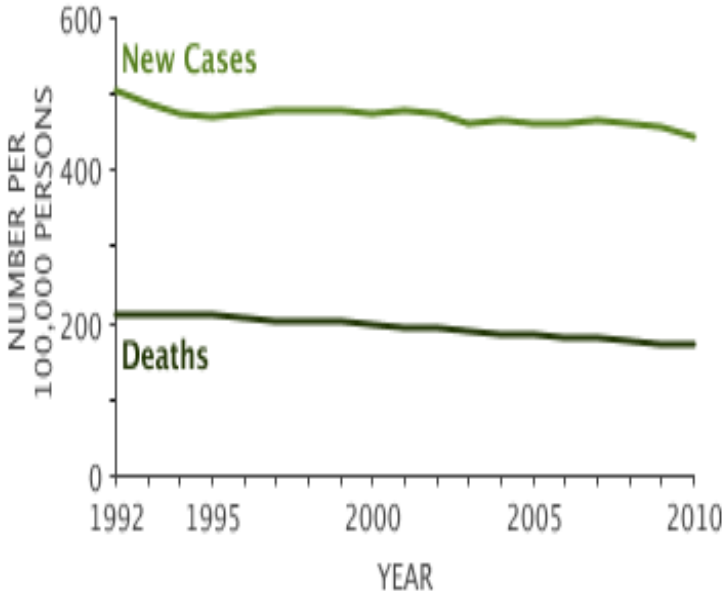
		CrCl							
		Cockcroft-Gault formula				aMDRD formula			
Variable*	All patients with normal SCR	<30 mL/min	30–59 mL/min	60–89 mL/min	≥90 mL/min	<30 mL/min	30–59 mL/min	60–89 mL/min	>90 mL/min
No. of patients	3903	8	641	1704	1510	0	255	1882	1766
%	100	0.2	16.4	43.7	38.7	0	6.5	48.2	37.7
Sex ratio (M:F)	0.49 (1289:2614)	(8:0)	0.23 (120:521)	0.52 (582:1122)	0.62 (576:934)	—	0.004 (1:254)	0.49 (616:1266)	0.61 (672:1094)
Age, y	57.6 ± 13.1	84.6 ± 8.8	67.6 ± 10.5	59.9 ± 11.1	50.6 ± 12.3	—	65.6 ± 11.6	60 ± 11.8	53.9 ± 13.5
Weight, kg	65.5 ± 13.9	45.1 ± 4	54.9 ± 8.9	63.2 ± 11.2	72.7 ± 14.6	—	64.5 ± 14	66.8 ± 14.1	64.3 ± 13.6
SCR, μmol/L	71.8 ± 15.7	95.4 ± 8.3	84.1 ± 13.2	74.5 ± 13.9	63.3 ± 13.8	—	95.7 ± 6.2	79.7 ± 11.2	59.9 ± 10.8
CrCl, mL//in	86.6 ± 29.4	27.2 ± 3.4	50.7 ± 7.1	74.8 ± 8.5	115.4 ± 23.6	—	54.4 ± 3.8	76.4 ± 8	113.6 ± 31.5

National Cancer Institute

Surveillance, Epidemiology, and End Results Program

Turning Cancer Data Into Discovery

Estimated New Cases in 2013	1,660,290
% of All New Cancer Cases	100.0%
Estimated Deaths in 2013	580,350
% of All Cancer Deaths	100.0%

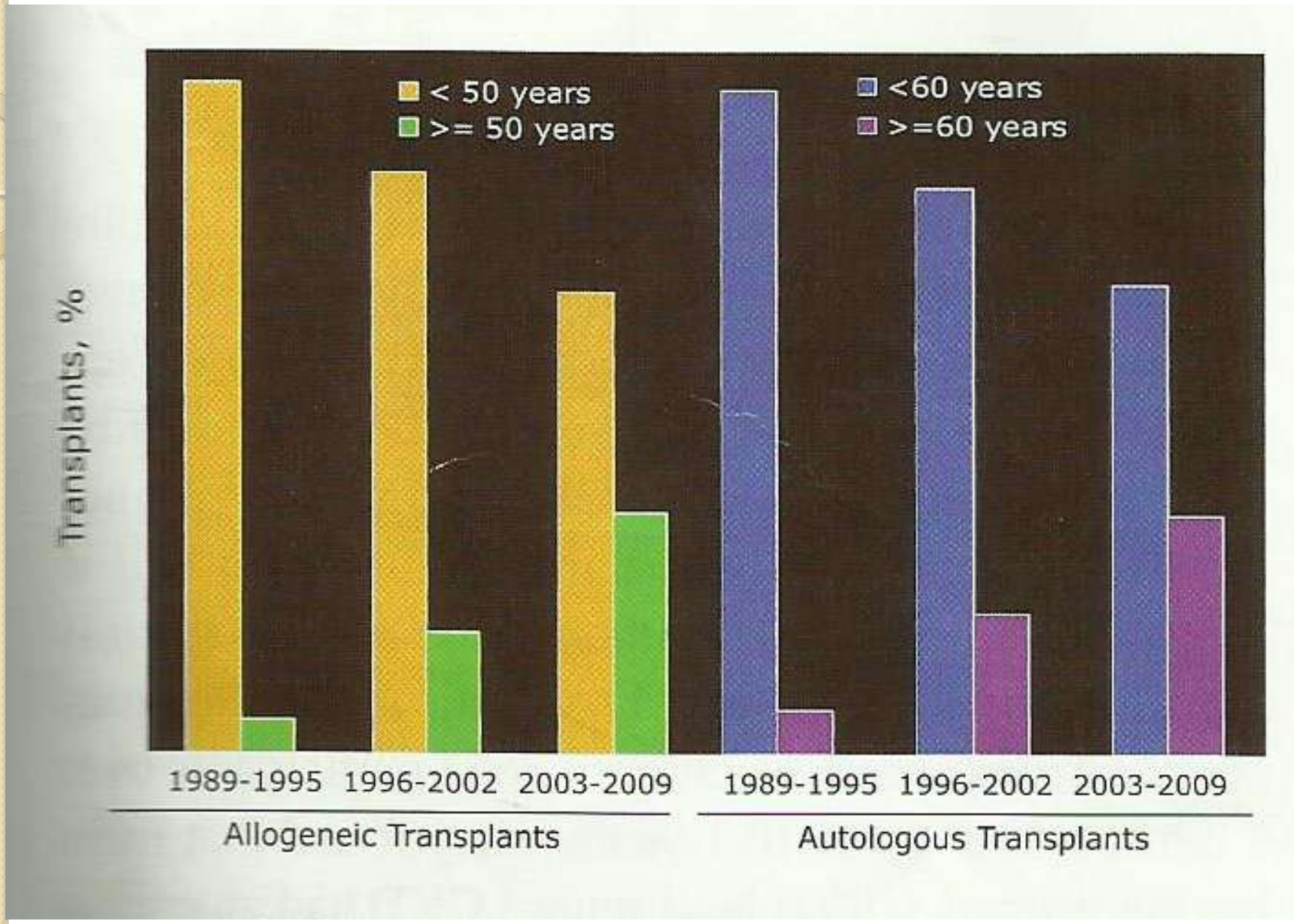


Percent Surviving 5 Years

65.8%

2003–2009

Number of New Cases and Deaths per 100,000: The number of new cases of all cancer sites was 463.0 per 100,000



Nephrology Self-Assessment Program - Vol 12, No 1, January 2013

Cancer & CKD

Mechanisms by Which CKD Might Be Associated With Increased Risk of Cancer Death

Mechanism	Example	Comment
The cancer itself causes CKD	Prostate cancer, uterine cervix cancer, myeloma	Important in clinical practice
Cancer and CKD have the same cause	Smoking	Causes bladder cancer and renovascular disease
	HCV infection	Causes liver cancer and glomerulonephritis
	Herbal nephrotoxins	Cause interstitial nephritis and urothelial cancers
	Analgesics	Analgesic nephropathy and urothelial cancers now rare
Drugs used in kidney disease cause cancer	Cyclophosphamide	Used in ANCA vasculitis and severe SLE nephritis; causes bladder cancer
	Pioglitazone	Used in type 2 DM; probably increases risk of bladder cancer
Drugs used in CKD increase tumor progression or other complications	ESAs	ESAs may decrease survival in patients with cancer
Delayed diagnosis of cancer	Delayed screening, eg, mammography	Opposite of lead-time bias; not proved to occur in CKD patients
Death is independent of the cancer	Death from CV disease	CKD is a known risk factor for CV death
CKD or associated morbidities limit treatment options	Cisplatin	Concern re increased nephrotoxicity and other adverse effects; optimal dosing difficult
	Bisphosphonates in myeloma	Concern re increased nephrotoxicity; optimal dosing difficult
	Hematopoietic cell transplantation	Low GFR of itself not an absolute contraindication, but comorbid conditions are often present, making this aggressive treatment high risk

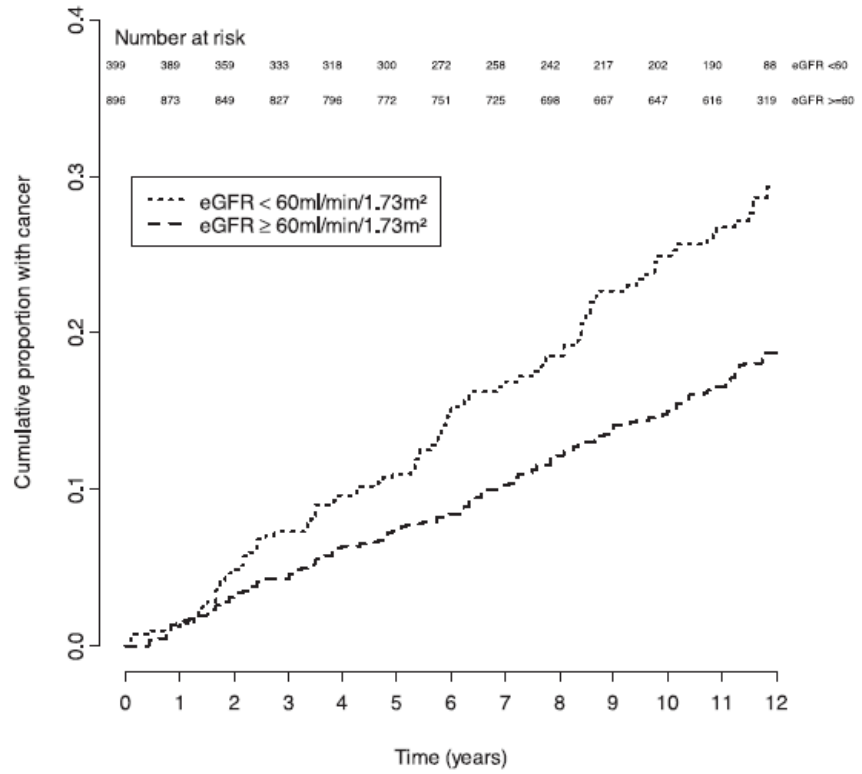
Am J Kidney Dis. 2014;63(1):7-9

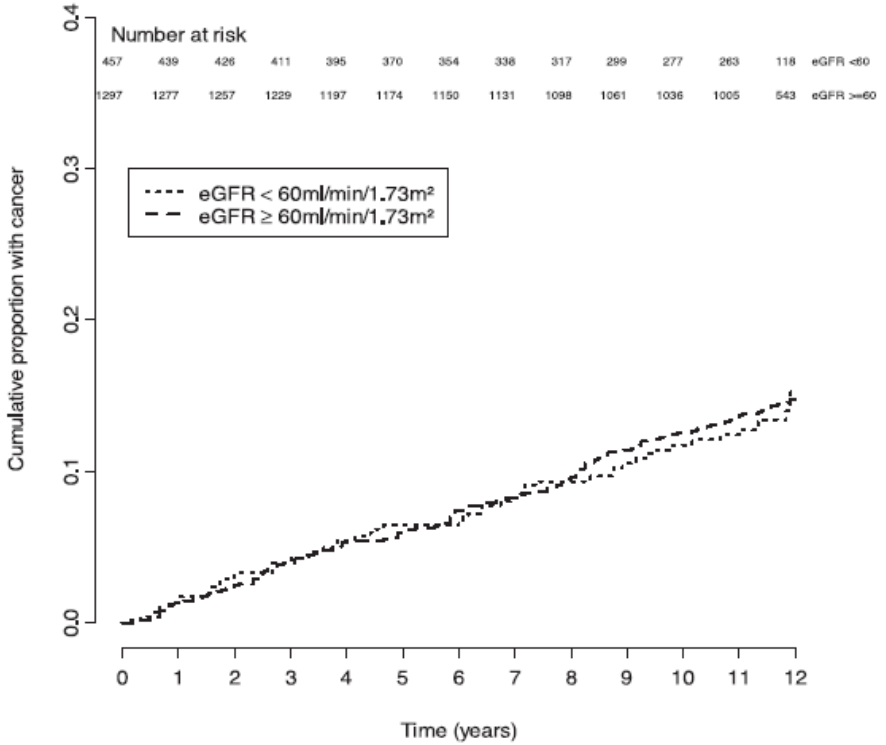
CLINICAL EPIDEMIOLOGY www.jasn.org

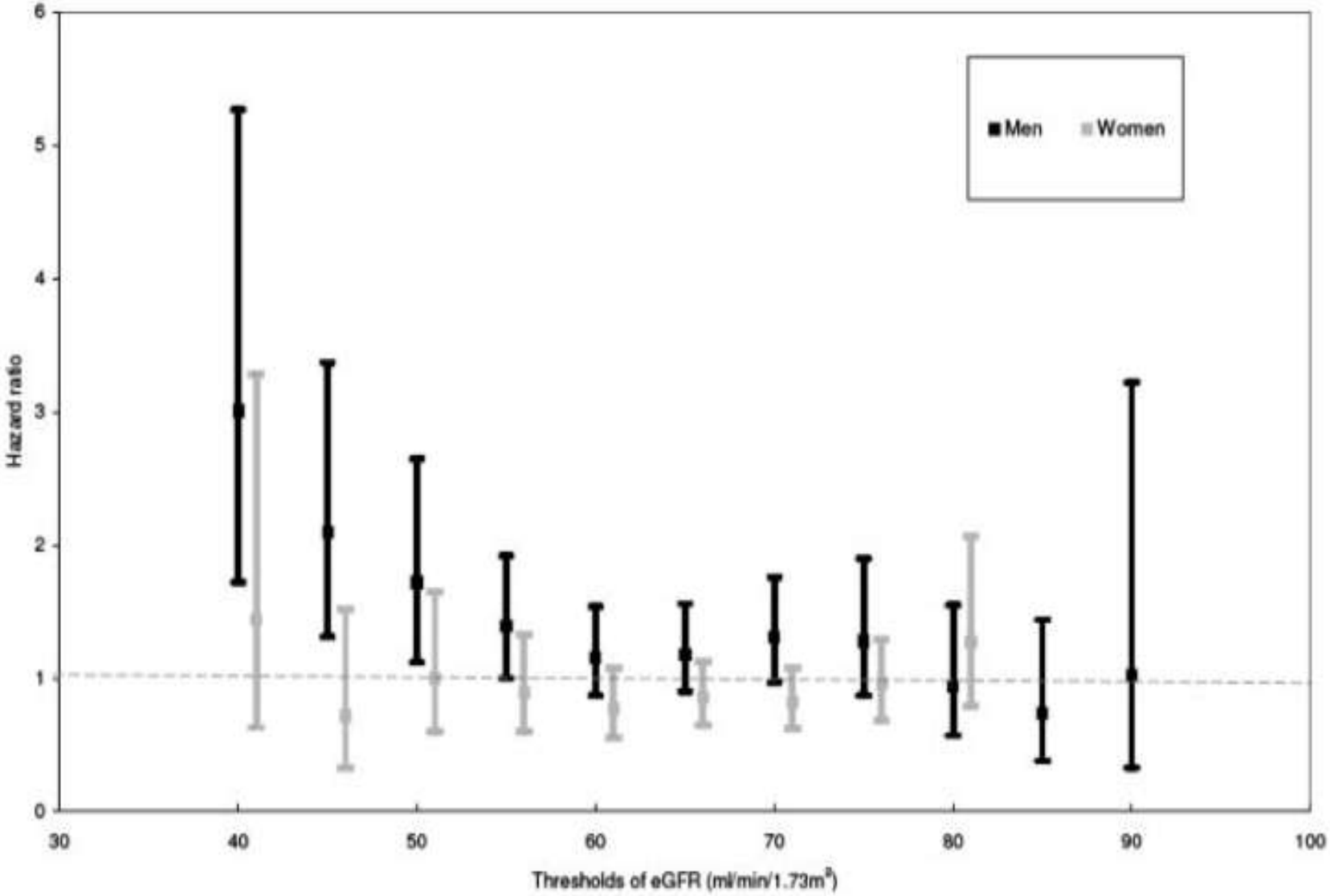
Association of CKD and Cancer Risk in Older People

Germaine Wong,*†‡ Andrew Hayen,† Jeremy R. Chapman,‡ Angela C. Webster,*†
Jie Jin Wang,§ Paul Mitchell,‖ and Jonathan C. Craig*†

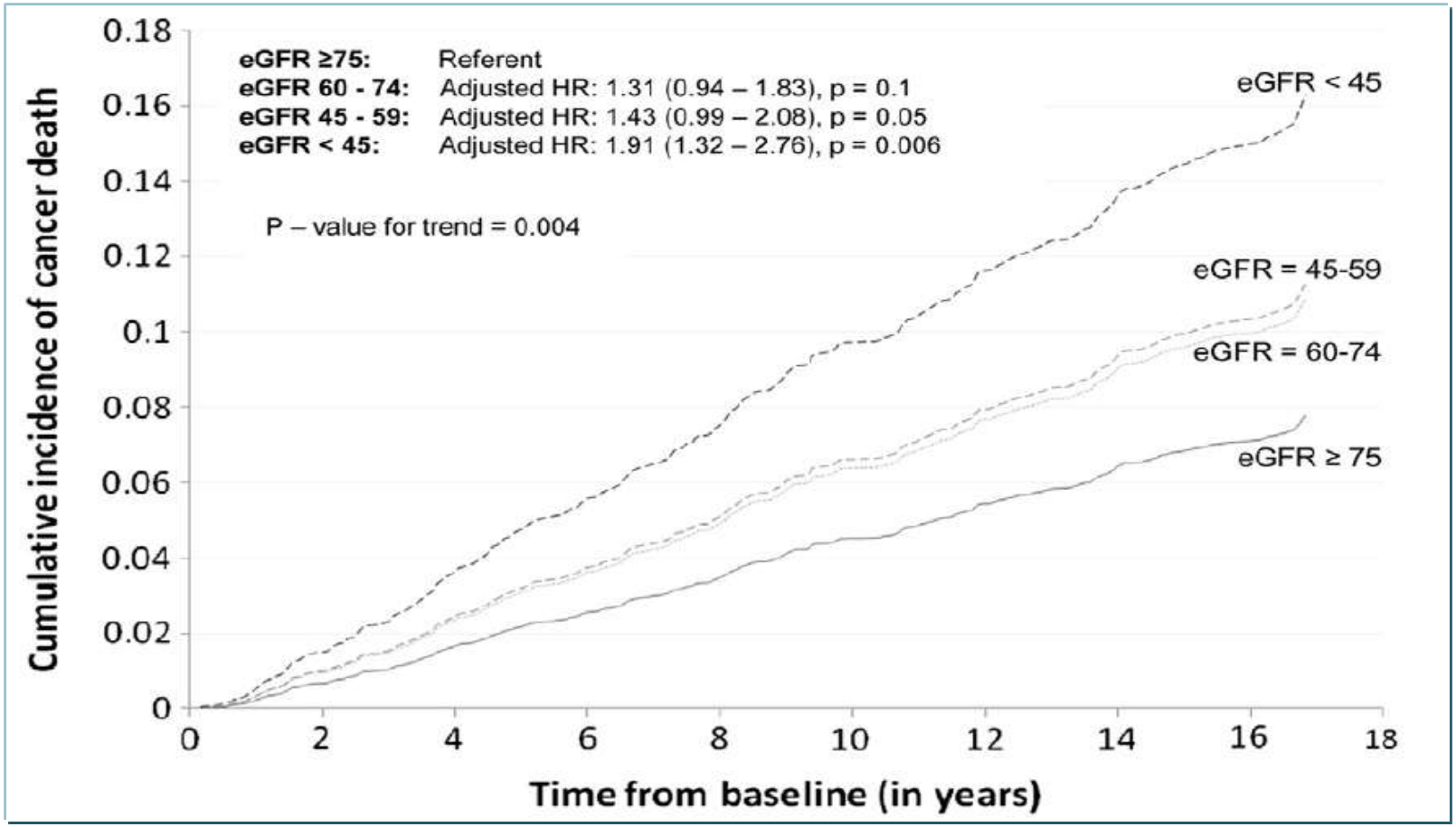
J Am Soc Nephrol 20: 1341–1350, 2009. doi: 10.1681/ASN.2008090998



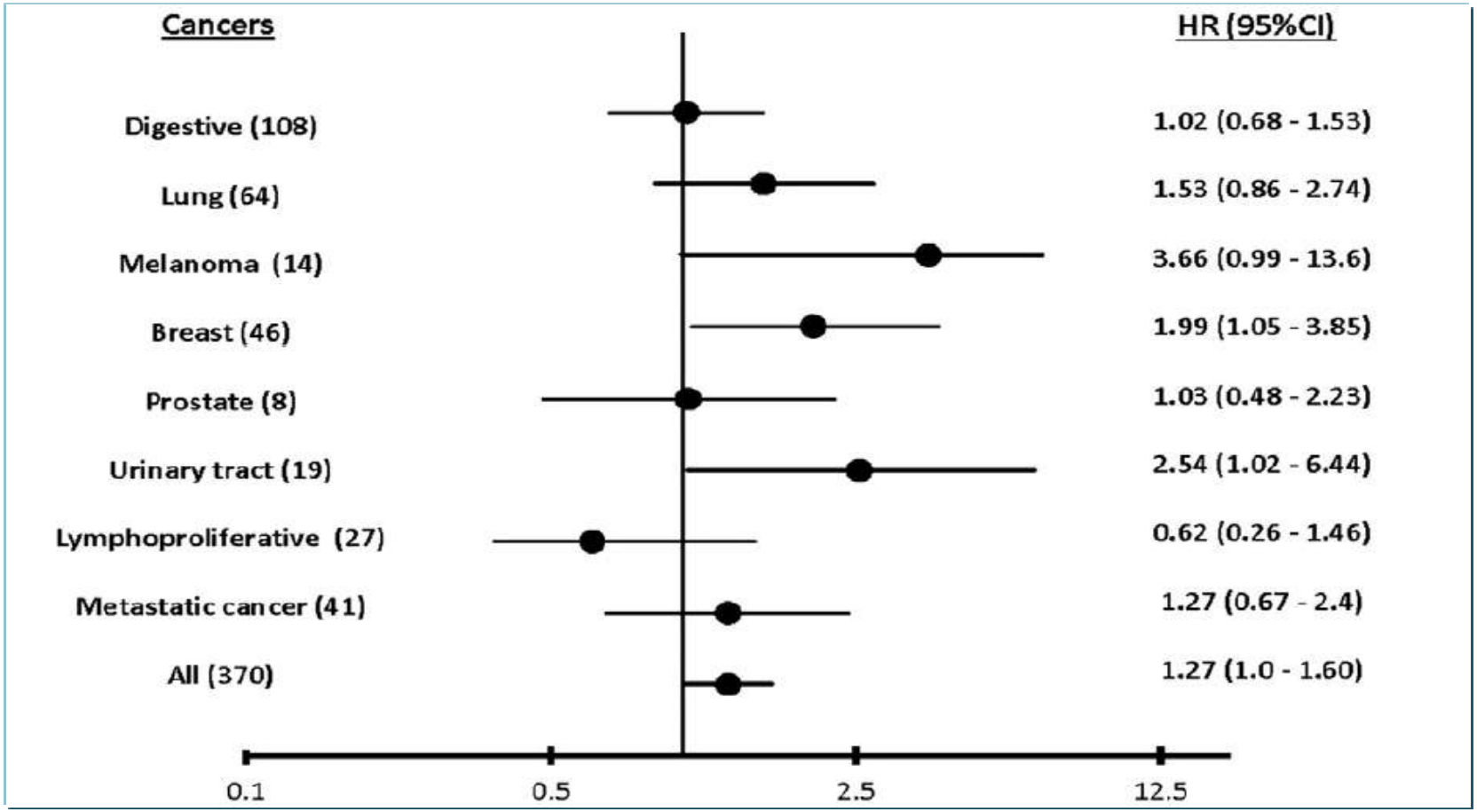



Men
Women
Hazard ratio
0
1
2
3
4
5
6
30
40
50
60
70
80
90
100
Thresholds of eGFR (ml/min/1.73m²)

CKD & Malignancy Mortality



Am J Kidney Dis 2014;63(1):23-30



Am J Kidney Dis. 2014;63(1):23-30

Cancer & ESRD

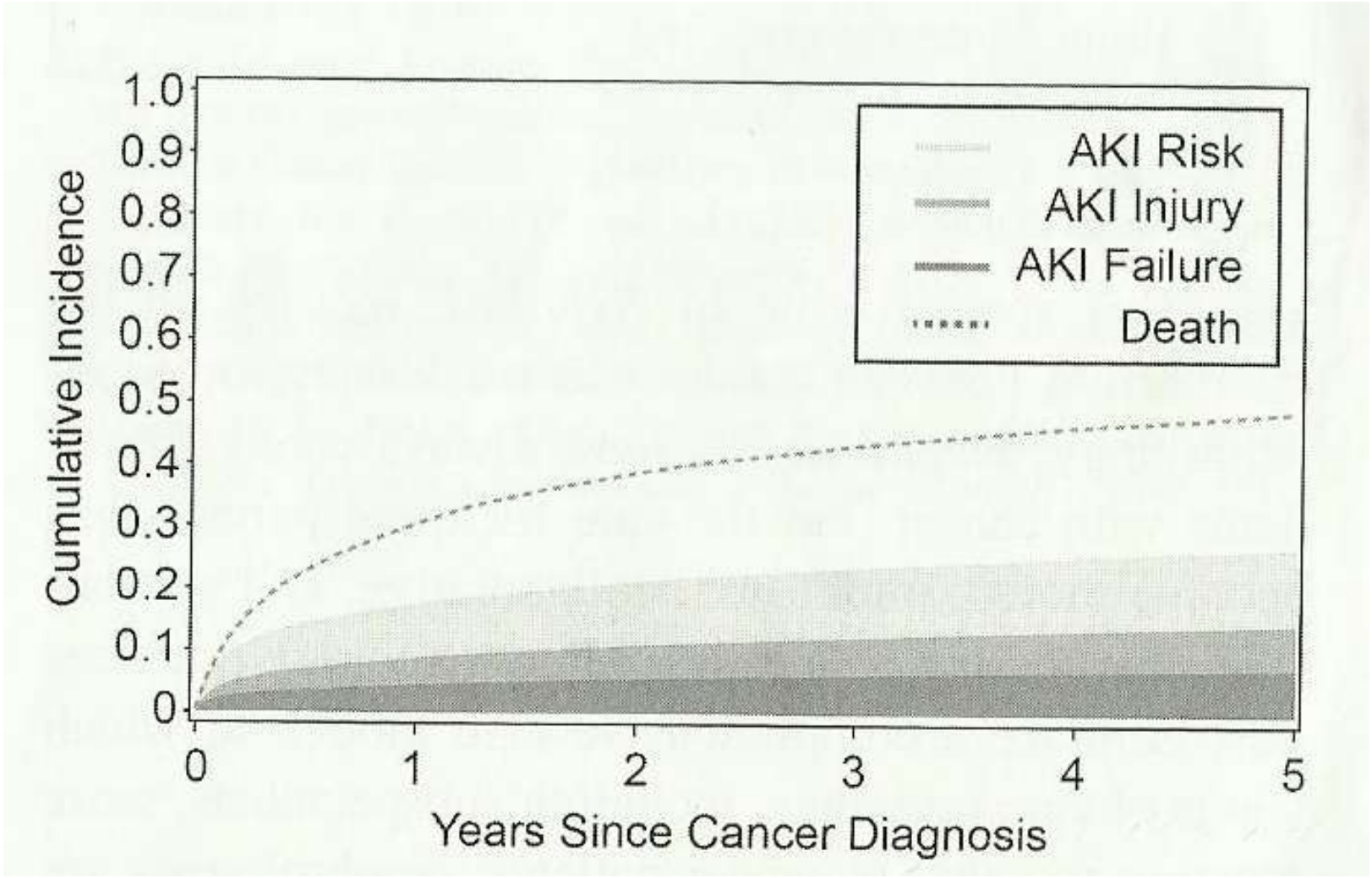
Incidence of reported ESRD, by primary diagnosis, 2007–2011 combined

by detailed primary diagnosis

COLUMN PERCENT	Total patients	Counts White	Black/ Af Am	N Am	Asian	Counts Hisp.	Non-Hisp.	% White	Black/ Af Am	N Am	Asian	% Hisp.	Non-Hisp.
Neoplasms/tumors	11,311	8,933	2,075	71	223	857	10,454	3	1	1	1	1	2
Renal tumor (malignant)	2,278	1,882	352	16	28	147	2,131	1	0	0	0	0	0
Urinary tract tumor (malignant)	737	614	109	*	*	49	688	0	0	*	*	0	0
Renal tumor (benign)	87	70	12	.	*	*	81	0	0	.	*	*	0
Urinary tract tumor (benign)	49	47	*	.	.	*	44	0	*	.	.	*	0
Renal tumor (unspecified)	264	206	46	*	*	22	242	0	0	*	*	0	0
Urinary tract tumor (unspecified)	175	145	25	*	*	25	150	0	0	*	*	0	0
Lymphoma of kidneys	178	145	24	*	*	15	163	0	0	*	*	0	0
Multiple myeloma	5,482	4,136	1,188	33	121	410	5,072	1	1	1	1	1	1
Other immuno prolif. neoplasms (inc. light chain neph.)	693	557	112	*	19	41	652	0	0	*	0	0	0
Amyloidosis	1,368	1,131	205	*	23	137	1,231	0	0	*	0	0	0

United States Renal Data System
2013 Annual Data Report

Cancer & AKI



Eur J Intern Med 22: 399-406, 2011.

VOLUME 24 · NUMBER 24 · AUGUST 20 2006

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

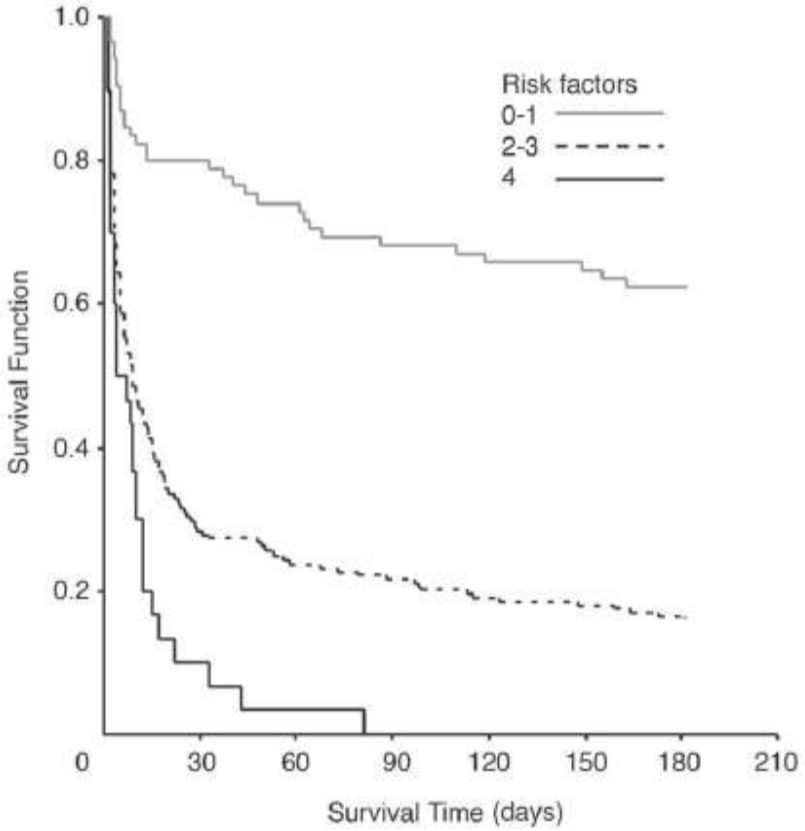
Prognosis of Critically Ill Patients With Cancer and Acute Renal Dysfunction

Márcio Soares, Jorge I.F. Salluh, Marilia S. Carvalho, Michael Darmon, José R. Rocco, and Nelson Spector

Table 3. Main Associated Factors of Acute Renal Dysfunction (N = 309)

	No.	%
Ischemia/shock	223	72
Sepsis	195	63
Radiocontrast/nephrotoxins	49	16
Urinary tract obstruction (cancer related)	23	7
Unilateral nephrectomy (cancer)	12	4
Acute tumor lysis syndrome	10	3
Multiple myeloma	9	3
Rhabdomyolysis	3	1
Unknown/other	15	5

NOTE. A patient could have more than one associated condition.



Box 31.1 Common Causes of Kidney Injury in Cancer Patients

Prerenal

Hypovolemia (poor fluid intake, vomiting, diarrhea, capillary leak syndrome with IL-2)
NSAIDs
Hypercalcemia
Hepatorenal syndrome (after HCT, massive infiltration by cancer cells)

Intrarenal

Glomerular

Membranous nephropathy
ANCA vasculitis
Amyloidosis
Light chain deposition disease
Collapsing glomerulopathy (pamidronate)

Tubulointerstitial

ATN due to sepsis, hypovolemia, IV contrast
ATN due to drugs (cisplatin, ifosfamide, zoledronate)
Acute cast nephropathy (myeloma)*
Tumor lysis syndrome (uric acid and calcium-phosphate deposition)*
Methotrexate*

Vascular

HUS/TTP (gemcitabine, mitomycin C, and other drugs; conditioning regimen for allogeneic HCT)

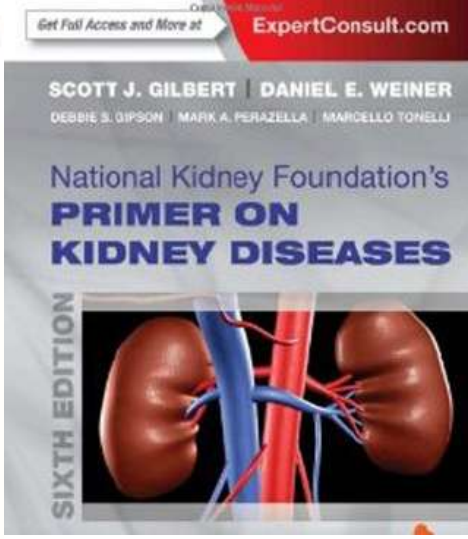
Postrenal

Obstruction of both urinary tracts by urological and nonurological cancers
Retroperitoneal fibrosis

Other

Bilateral nephrectomy (renal cancer)
Massive infiltration of kidneys by lymphoma

*Associated with both tubular injury and tubular obstruction.



Cancers with highest AKI risk

- Kidney cancer
- Multiple Myeloma
- Liver cancer
- Acute leukemia and lymphoma

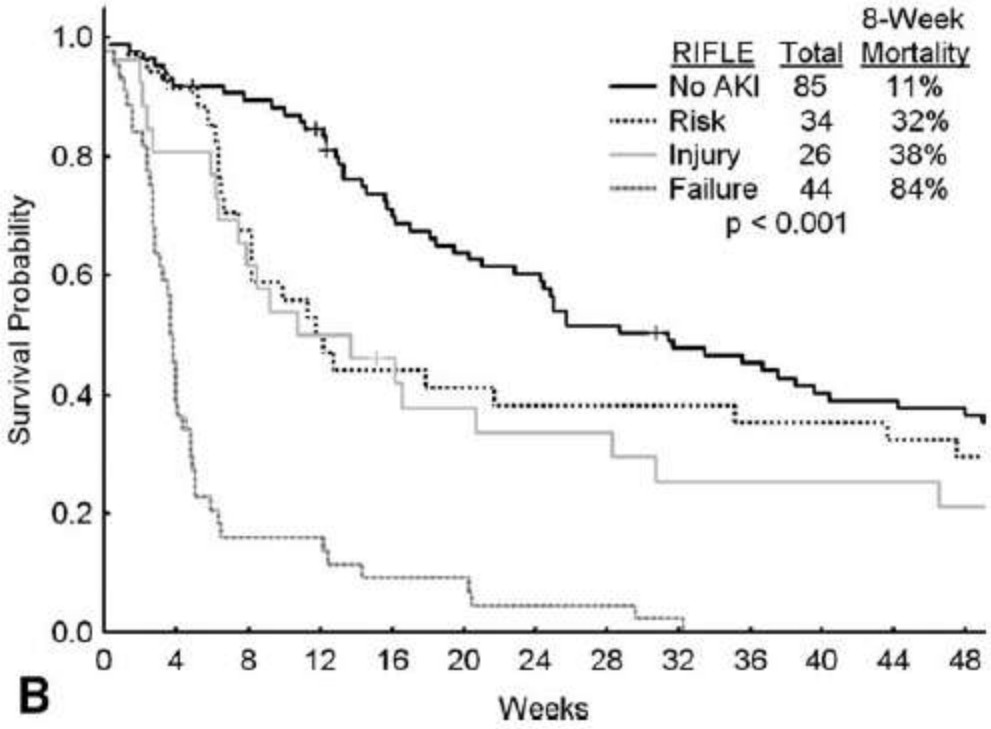
Original Article

Predictors and Outcome of Acute Kidney Injury in Patients With Acute Myelogenous Leukemia or High-Risk Myelodysplastic Syndrome

Amit Lahoti, MD[1]; Hagop Kantarjian, MD[2]; Abdulla K. Salahudeen, MD[1]; Farhad Ravandi, MD[2]; Jorge E. Cortes, MD[2]; Stefan Faderl, MD[2]; Susan O'Brien, MD[2]; William Wierda, MD[2]; and Gloria N. Mattiuzzi, MD[2]

Cancer September 1, 2010

	No. of Patients (%)	8-Week Mortality
No AKI	345 (64)	3.8%
RIFLE-Risk	81 (15)	13.6%
RIFLE-Injury	51 (10)	19.6%
RIFLE-Failure	60 (11)	61.7%



KIDNEY PROPLEMS IN SPECIAL ONCOLOGICAL SITUATIONS

Kidney disease in HCT

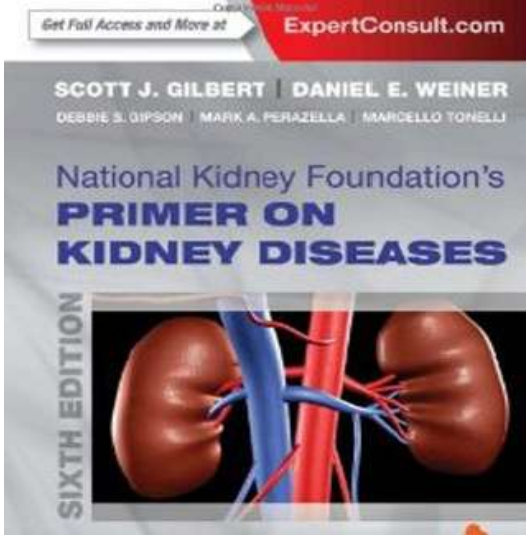


Table 31.4 Overview of HCT Types and Their Kidney Complications

	Allogeneic Myeloablative	Autologous Myeloablative	Allogeneic Nonmyeloablative
Cancers treated	Many leukemias, lymphomas, myelodysplastic syndromes	Lymphomas, multiple myeloma	As for allogeneic myeloablative
Intensity of conditioning regimen	High	High	Low
GVHD after HCT	Yes (CNIs used as prophylaxis)	No	Yes (CNIs used as prophylaxis)
AKI after HCT	Common; sometimes severe	Rare	Common; rarely severe
Causes of AKI (usually first 3 months)	VOD, shock syndromes, nephrotoxic drugs, CNIs	Shock syndromes, nephrotoxic drugs, occasionally VOD	CNIs
CKD after HCT	Common	Common (but not severe)	Mild forms probably common
Causes of CKD	Irreversible AKI, renal TMA, CNIs; membranous nephropathy	Irreversible AKI; recurrence of original disease (myeloma)	Irreversible AKI, CNIs, membranous nephropathy

AKI, Acute kidney injury; *CKD*, chronic kidney disease; *CNI*, calcineurin inhibitors; *GVHD*, graft-versus-host disease; *HCT*, hematopoietic cell transplantation; *TMA*, thrombotic microangiopathy; *VOD*, venoocclusive disease.

AKI after HCT

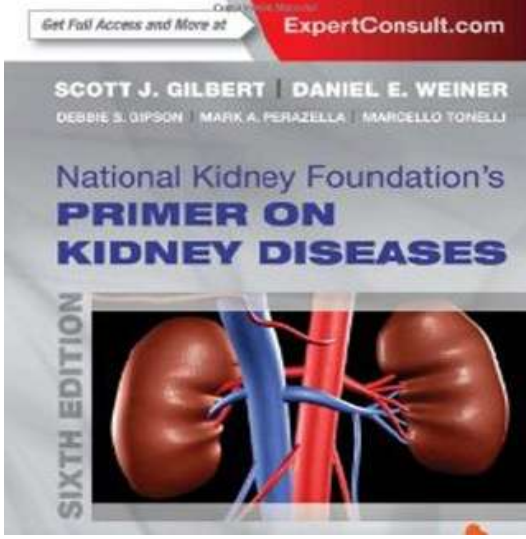
- Early onset (<30 days)
  - Sepsis
  - Hypotension
  - Hypovolemia (vomiting and diarrhea)
  - Nephrotoxic agents
    - Acyclovir
    - Allopurinol
    - Amphotericin B
    - Angiotensin-converting enzyme inhibitors
    - Angiotensin receptor blockers
    - Calcineurin inhibitors
    - Contrast dye
    - Methotrexate
    - NSAIDs
  - Tumor lysis syndrome
  - Hepatic sinusoidal obstruction syndrome
- Late onset (>3 months)
  - Thrombotic microangiopathy
  - Calcineurin inhibitor toxicity

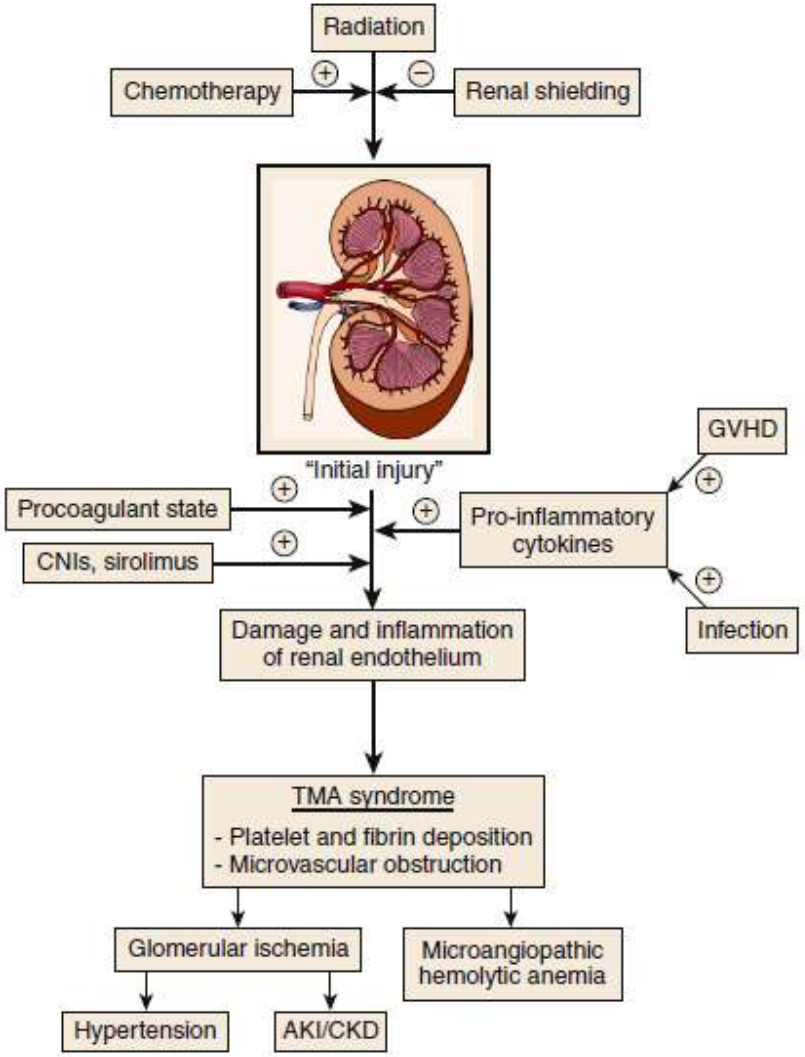
Clin J Am Soc Nephrol 7: 1692–1700, October, 2012

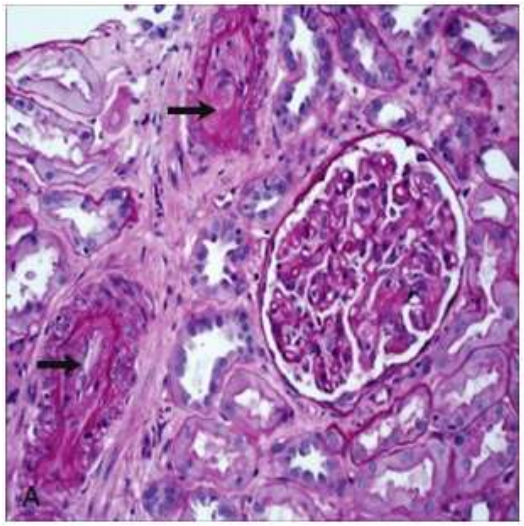
VOD

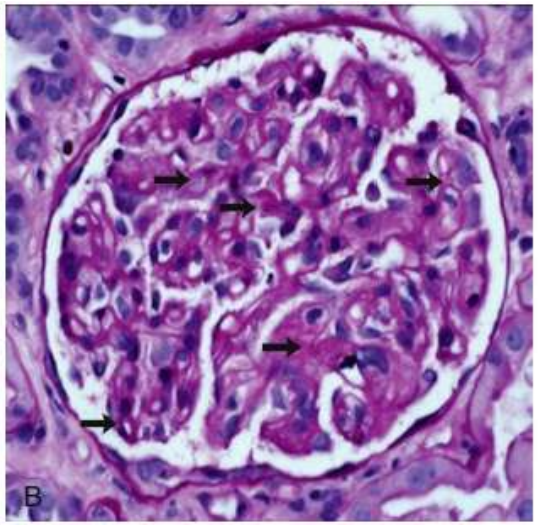
- Due to conditioning regimens; cyclophosphamide, busalphan and total body irradiation.
- Edema, salt retension, weight gain, hepatomegally and reversal of flow in the portal vein.
- leads to AKI similar to hepatorenal syndrome.

TMA after HCT





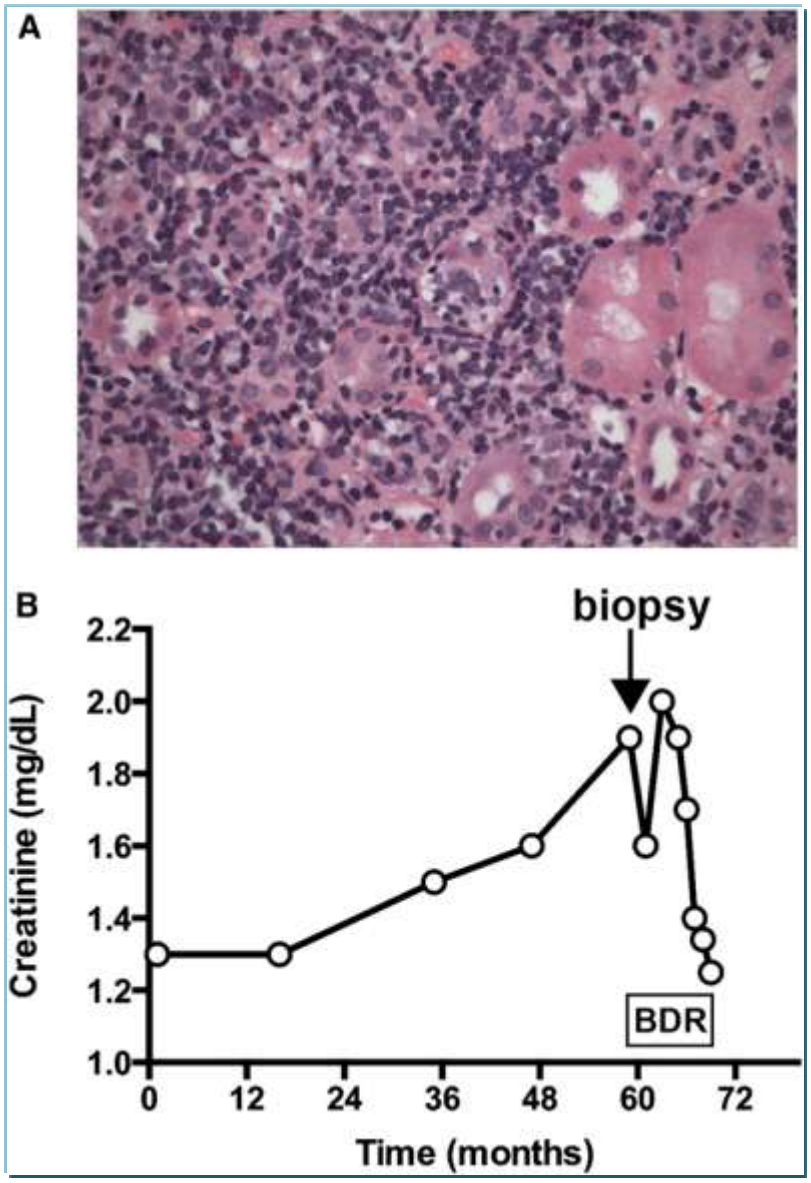




Renal involvement in leukemia and lymphoma

1. **Obstructive uropathy**
2. **Infiltration of renal parenchyma**
3. **Amyloidosis**
4. **Therapy associated**
5. **Urate nephropathy**
6. **Glomerulopathy**
7. **Disseminated intravenous coagulation**

LIK



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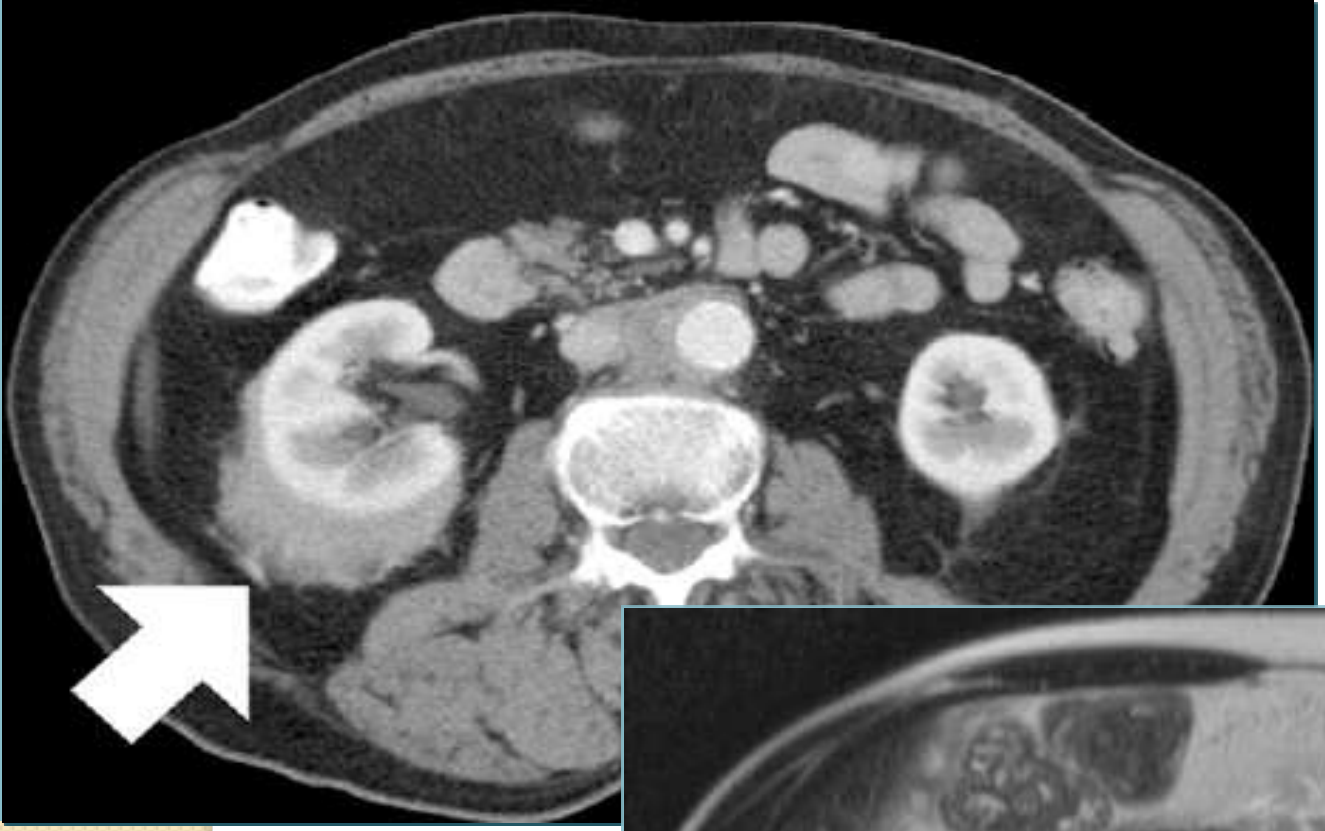
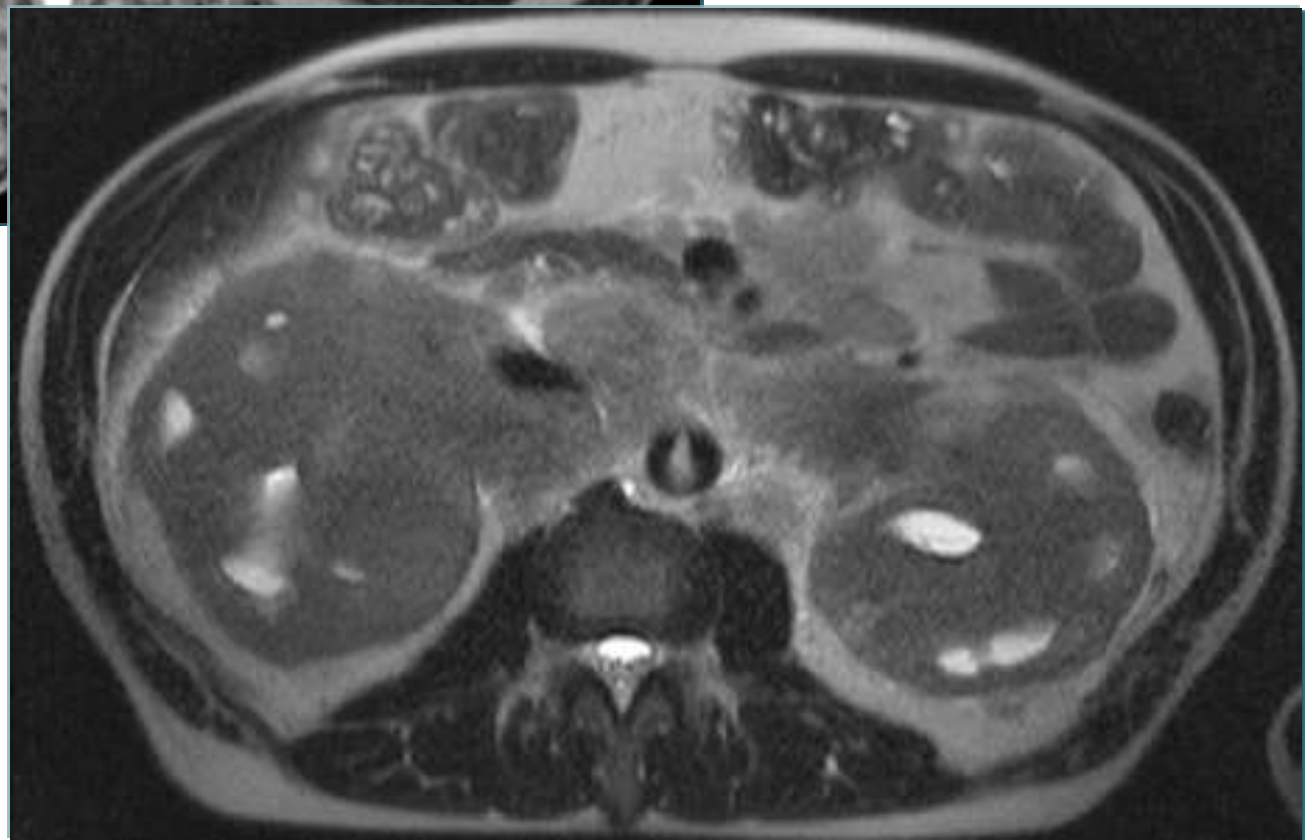




Renal affection in Multiple myeloma

Mechanisms of renal failure in plasma cell dyscrasias: Ig-dependent and -independent

Mechanism	Details
Ig-independent mechanisms	
Volume depletion	Can cause prerenal azotemia and acute tubular necrosis and/or contribute to cast nephropathy
Sepsis	
Hypercalcemia	Can cause AKI directly or contribute to cast nephropathy
Tumor lysis syndrome	Uric acid or phosphate nephropathy
Medication toxicity	Zoledronate: rare cause of acute renal failure Pamidronate: rare cause of collapsing focal and segmental glomerulosclerosis Nonsteriodal anti-inflammatory drugs, angiotensin converting enzyme inhibitor, angiotensin receptor blocker, loop diuretics, or iodinated contrast may precipitate cast nephropathy
Direct parenchymal invasion by plasma cells	Rare cause; associated with advanced or aggressive myeloma
Pyelonephritis	Rare cause; multifactorial from immunodeficiency and deficient Ig and chemotherapy from myeloma

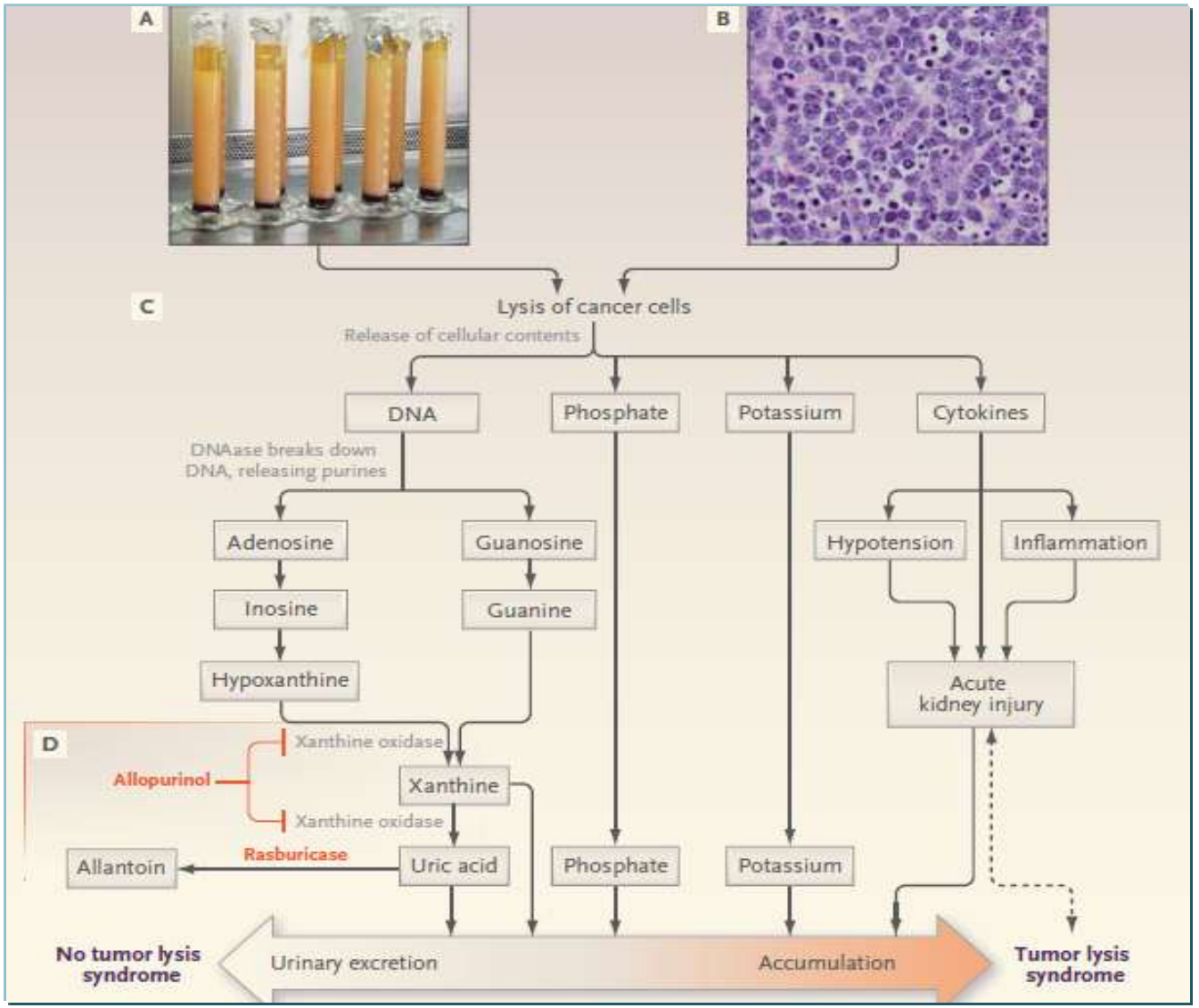
Clin J Am Soc Nephrol 8: 2007–2017, November, 2013

Renal Pathology in Patients with Multiple Myeloma

Histological Finding	Prevalence
Myeloma kidney *(Myeloma cast nephropathy)*	30%-50%
Interstitial nephritis/fibrosis without cast nephropathy	20%-30%
Amyloidosis	10%
Light chain deposition disease	5%
Acute tubular necrosis	10%
Other (urate nephropathy, tubular crystals, hypercalcemia, FSGS)	5%

Comprehensive textbook of Nephrology, 2010 ed

TLS



N Engl J Med 2011;364:1844-54.

Definitions of laboratory TLS and clinical TLS proposed by Cairo and Bishop and modified by Howard *et al*.

Laboratory TLS	Clinical TLS
(Requires ≥2 laboratory abnormalities)	(Requires laboratory TLS features plus any clinical finding below)
Hyperuricemia (uric acid ≥8 mg/dl)	AKI≥
Hyperphosphatemia (>4.5 mg/dl in adults; >6.5 mg/dl in children)	Stage I (AKIN criteria)≥ R (RIFLE criteria)
Hyperkalemia (potassium >6.0 mEq/L)	Cardiac dysrhythmia, sudden death
Hypocalcemia (corrected serum calcium <7.0 mg/dl, or ionized calcium <1.12 mg/dl)	Cardiac dysrhythmia, sudden death, seizure, tetany, carpopedal spasm, bronchospasm, laryngospasm, hypotension

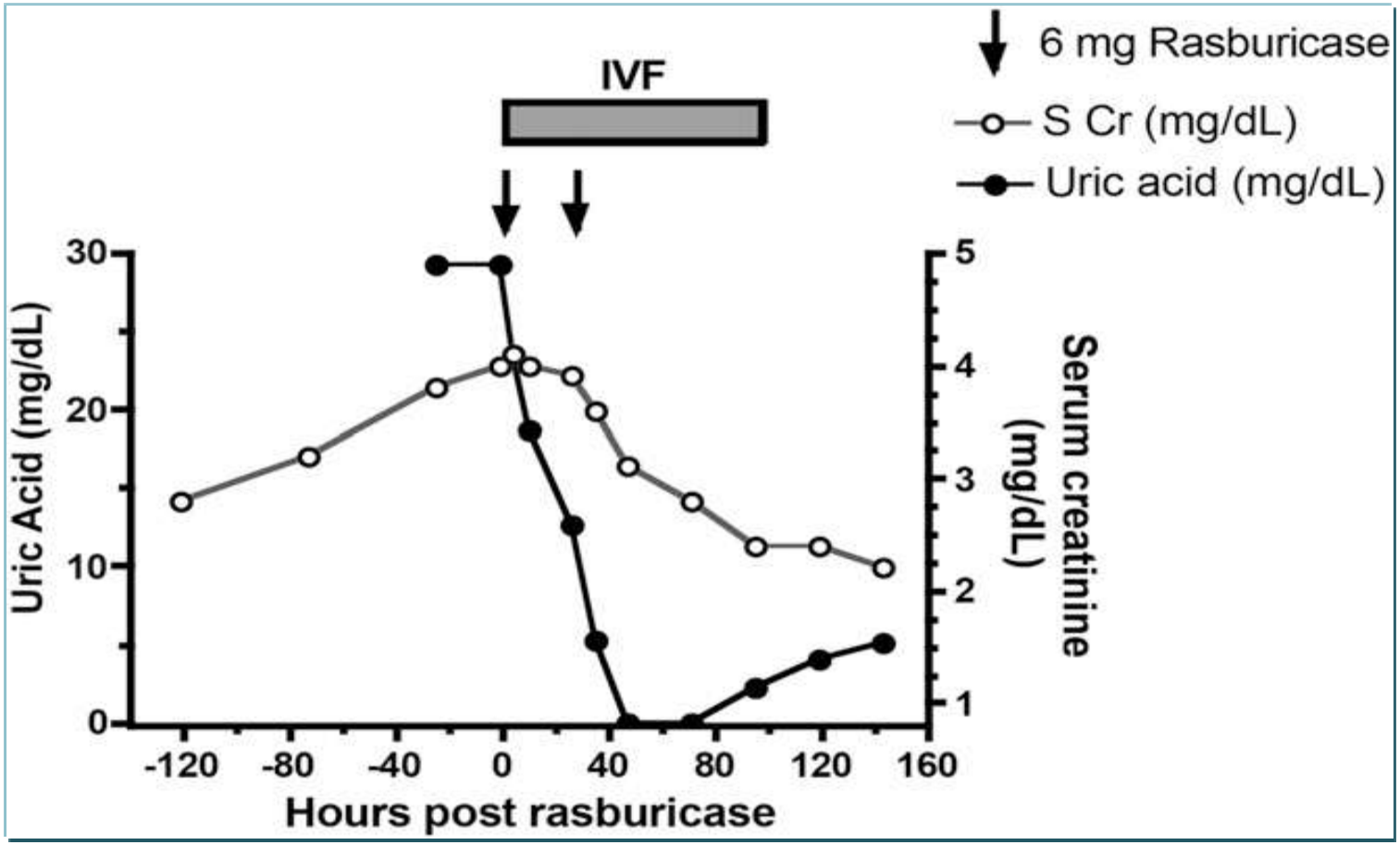
AKIN, Acute Kidney Injury Network. Data are from the following studies: Cairo MS, Bishop M: Tumour lysis syndrome: New therapeutic strategies and classification. *Br J Haematol* 127: 3–11, 2004; and from Howard SC, Jones DP, Pui CH: The tumor lysis syndrome. *N Engl J Med* 364: 1844–1854, 2011.

N Eng J Med 364: 1844-1854, 2011

Risk factors that predispose to TLS

Risk Factor	Description
Tumor mass	Large tumor mass, extensive metastases
	Organ (kidney, liver, bone marrow) infiltration
	High rate of cell proliferation: LDH, WBC count, etc.
	Cancer cell type: hematological versus nonhematological
Acute cell lysis potential	Chemosensitivity
	Intensity of chemotherapy
Underlying conditions	Underlying CKD
	Hypotension
	Volume depletion
	Nephrotoxin exposure

N Eng J Med 364: 1844-1854, 2011



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Glomerular diseases

Endothelial damage (TMA)

Mitomycin C, gemcitabine, anti-VEGF agents, TKI, mTOR inhibitors, calcineurin inhibitors

Epithelial (podocyte) damage

Collapsing FSGS: pamidronate, mTOR inhibitors, calcineurin inhibitors, interferons α, β, and γ, adriamycin

FSGS NOS: interferons α, β, and γ, calcineurin inhibitors, mTOR inhibitors, daunorubicin

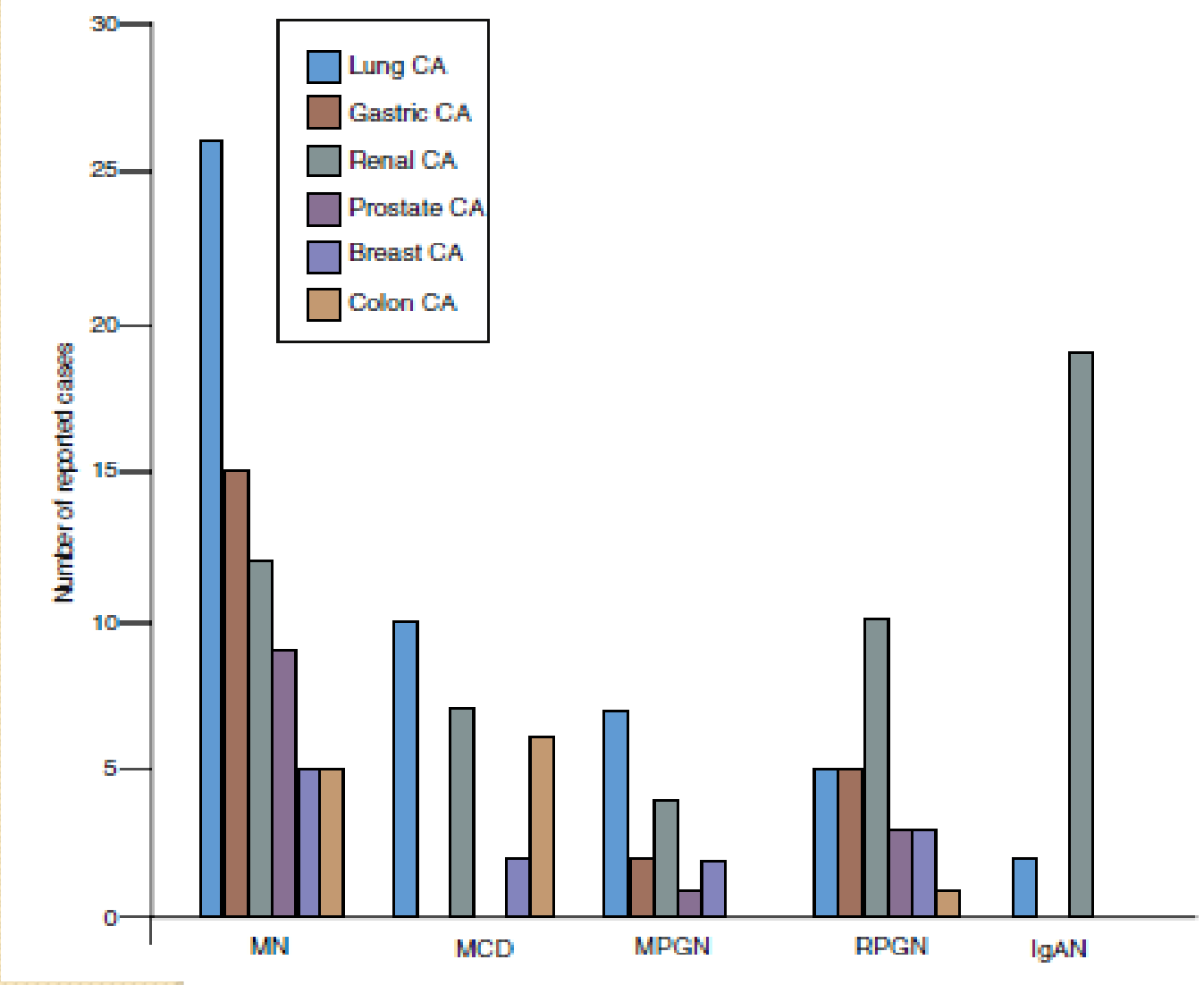
Minimal change disease: pamidronate, interferons α, β, and γ, daunorubicin

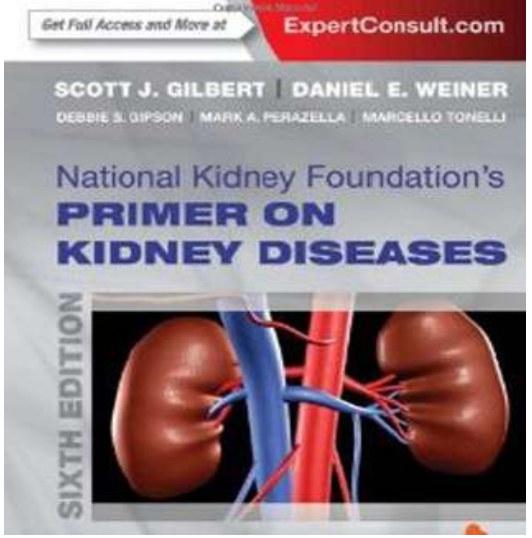
MPGN: anti-VEGF agents

Crescentic GN: GM-CSF

Lupus-like nephritis: ipilimumab

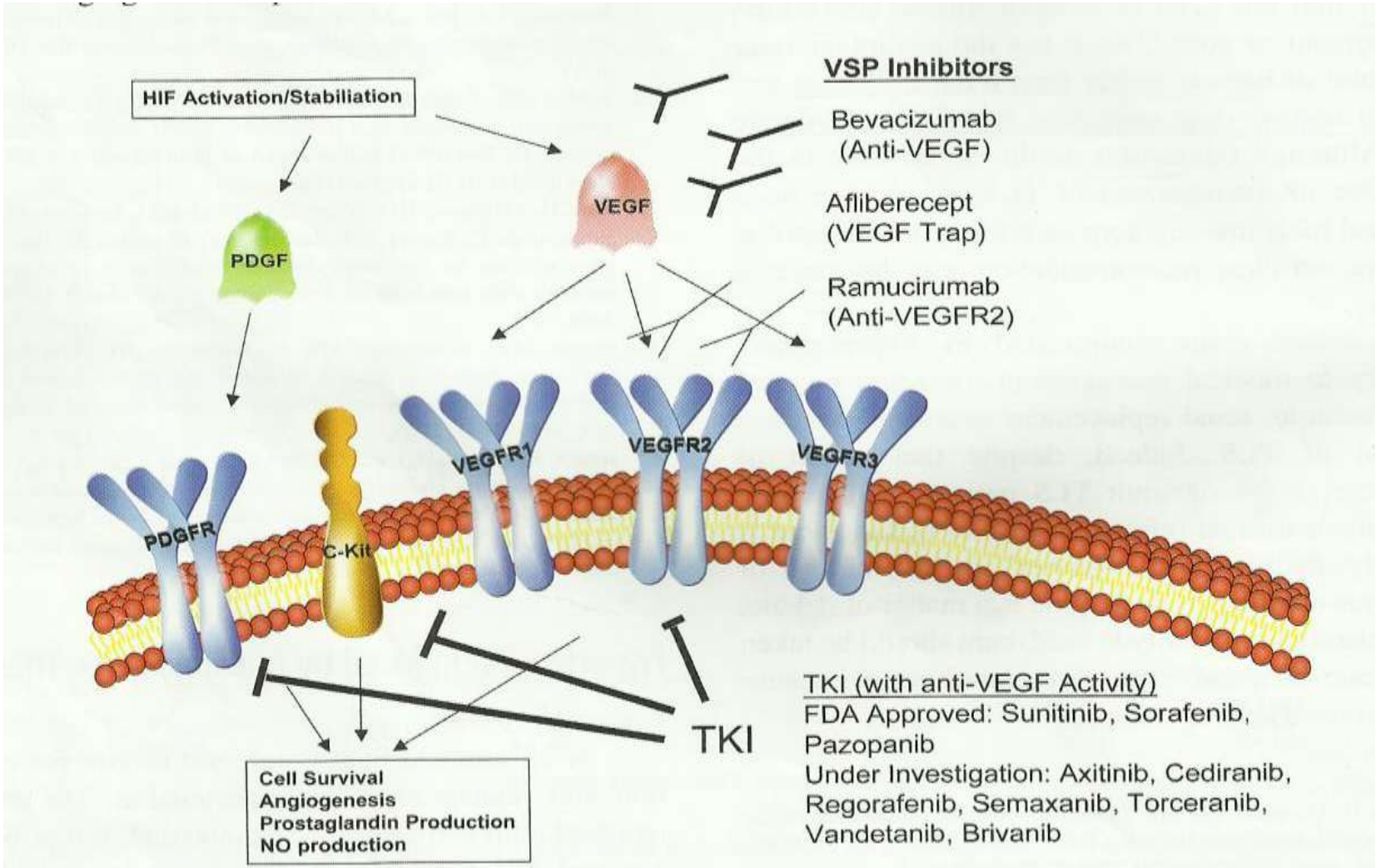
Kidney International (2013) 84, 34–44;





Nat Rev Nephrol 7:85-95, 2011.

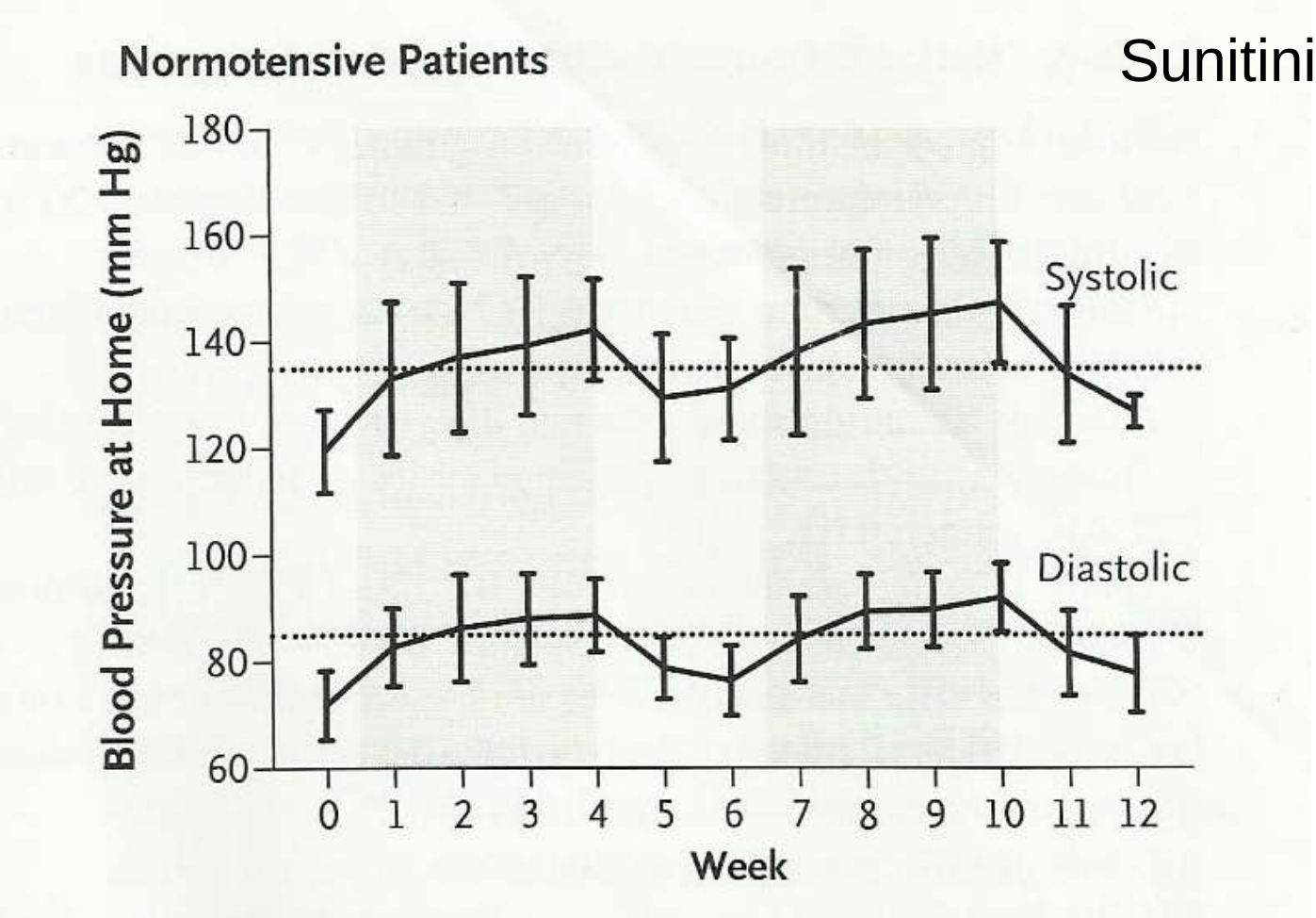
COMPLICATIONS OF ANTIANGIOGENIC THERAPIES



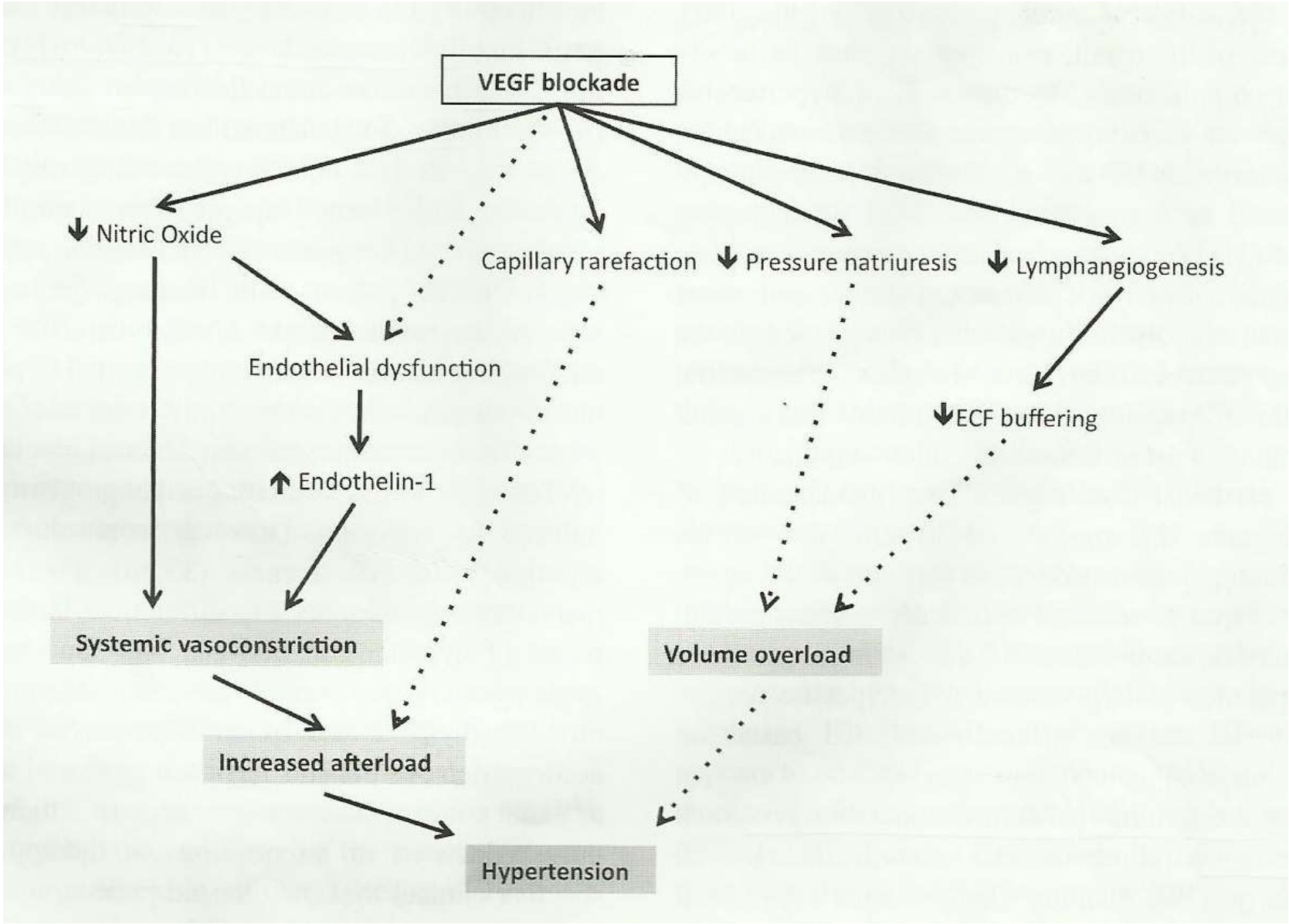
Circulation 124: 1687-1691, 2011.

Hypertension

Sunitinib



N Eng J Med 358: 95-97, 2008.



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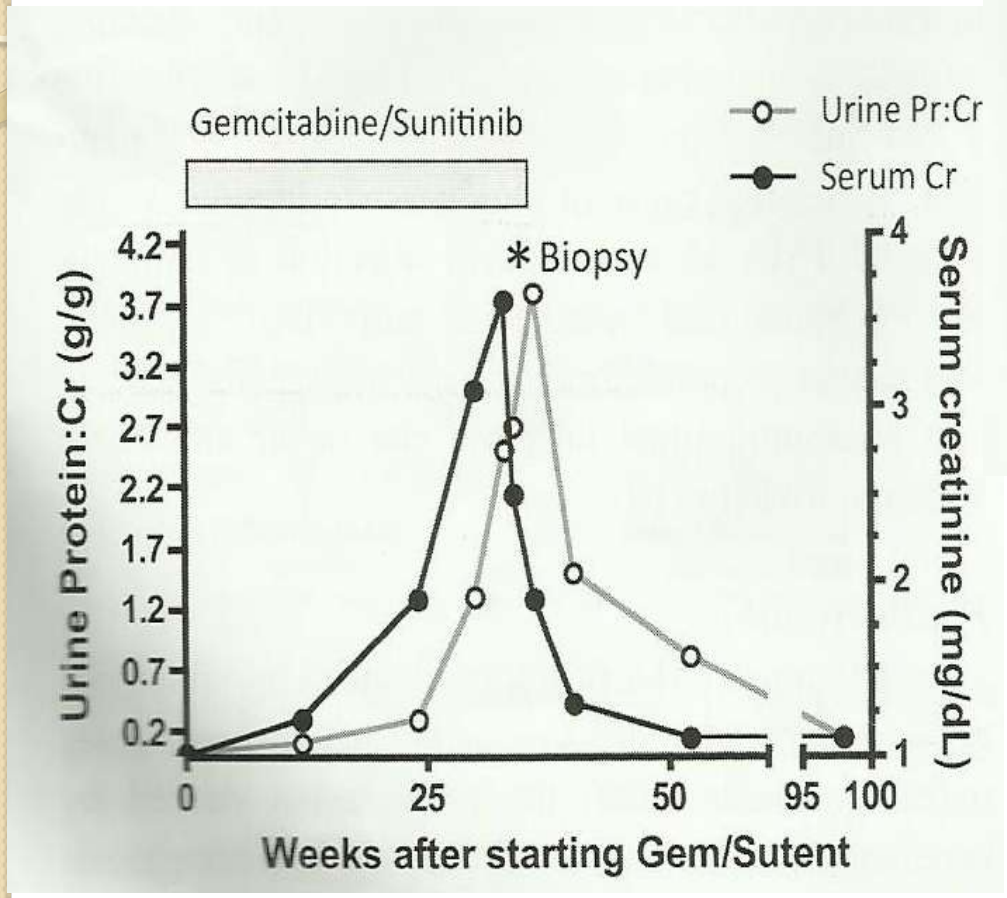
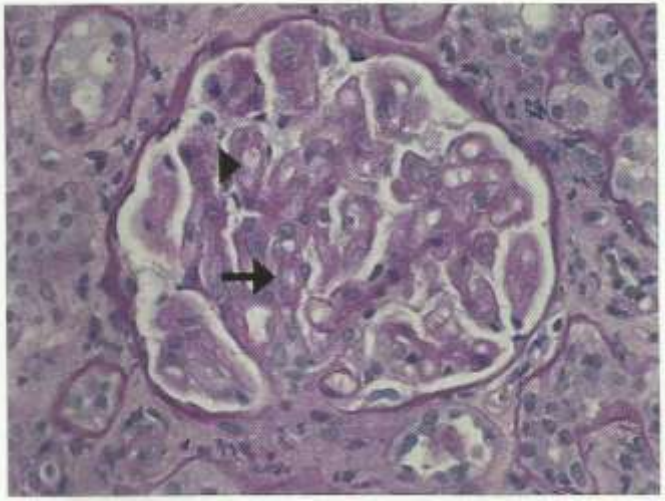
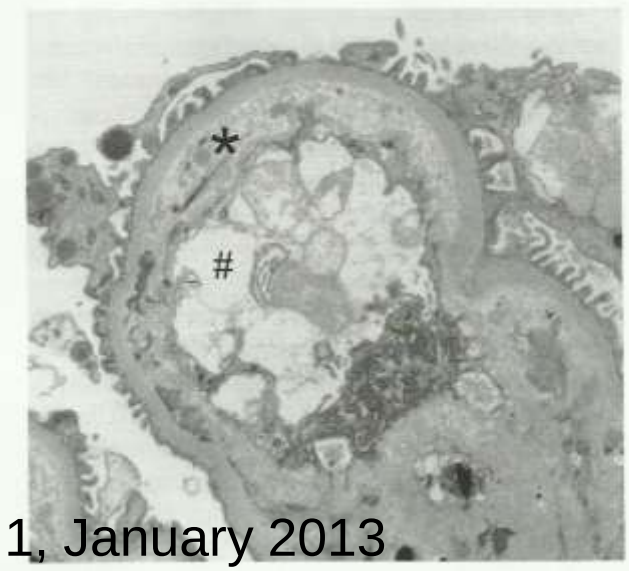
TMA


Gemcitabine/Sunitinib
Urine Pr:Cr
Serum Cr
* Biopsy
Urine Protein:Cr (g/g)
4.2
3.7
3.2
2.7
2.2
1.7
1.2
0.7
0.2
Serum creatinine (mg/dL)
4
3
2
1
0
25
50
95
100
Weeks after starting Gem/Sutent

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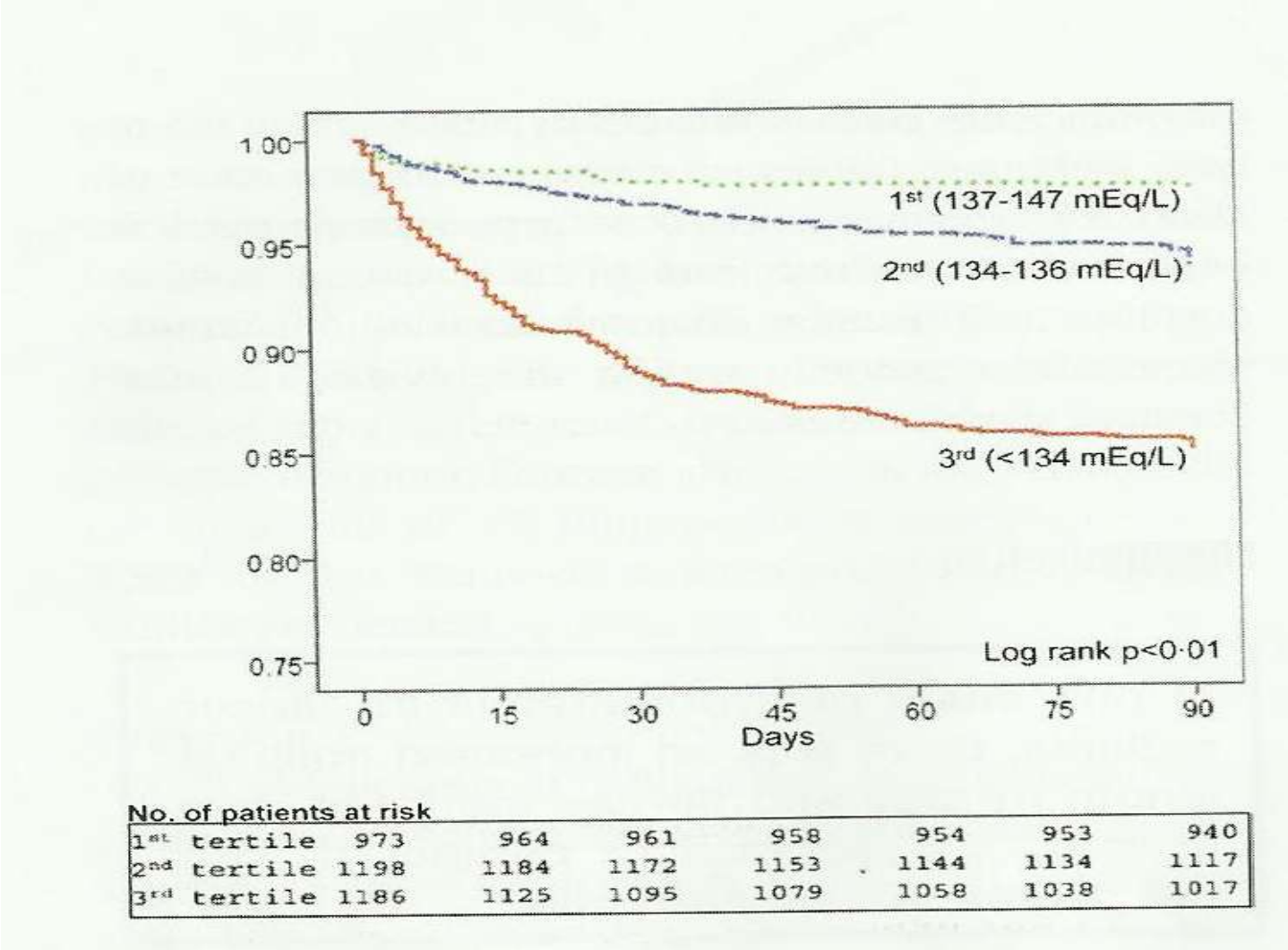
Electrolyte disturbance
1. Hyponatremia



No. of patients at risk

1st tertile	973	964	961	958	954	953	940
2nd tertile	1198	1184	1172	1153	1144	1134	1117
3rd tertile	1186	1125	1095	1079	1058	1038	1017

Am J Kidney Dis 59: 222-228, 2012.

2. Hypercalcemia

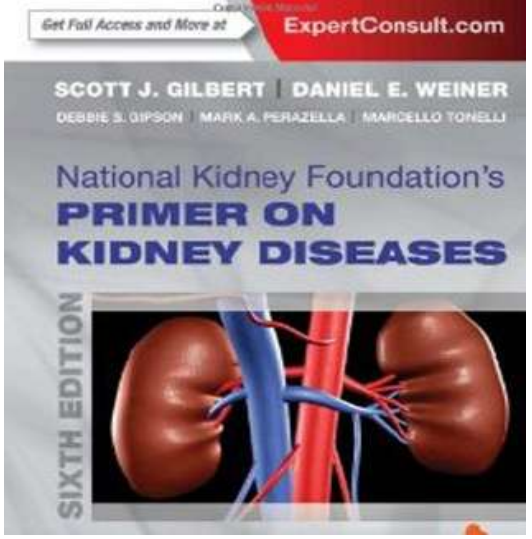


Table 31.1 Causes of Hypercalcemia in Individuals With Cancer

Type	Proportion	Bone Metastases	Mediator(s)	Typical Cancers
Humoral hypercalcemia of malignancy	80%	Minimal	PTHrp	Squamous cell (of lung, head/neck, cervix), ovarian cell, renal cell
Local bone breakdown	20%	Common and extensive	Cytokines, chemokines	Multiple myeloma, breast cancer, lymphoma
Excess 1,25 vitamin D_3	<1%	Variable	1,25 vitamin D_3	Lymphomas
Excess (ectopic) PTH	<1%	Variable	PTH	Variable

Modified from Stewart AF: Hypercalcemia associated with cancer, N Engl J Med *352:373, 2005.*
PTH, Parathyroid hormone; *PTHr,* parathyroid hormone–related peptide.

3. Hypokalemia

Cause	Mechanism
Pseudohypokalemia	
Marked leukocytosis	Transcellular shift into white blood cells during blood storage at room temperature, typically in acute myeloid leukemia
Redistribution	
Granulocyte-macrophage colony-stimulating factor	Rapid uptake of potassium during robust myelopoiesis
Nonrenal losses	
Villous adenoma	Chronic watery diarrhea
Vasoactive intestinal peptide-oma	Chronic watery diarrhea, may be part of multiple endocrine neoplasia type 1
Zollinger-Ellison syndrome	Gastrin-induced profuse diarrhea

Renal losses	
ACTH secreting tumor	Mineralocorticoid excess induces potassium secretion
Lysozymuria in myelomonocytic leukemia	Lysozyme-induced tubular injury
Anti-EGF receptor antibodies (Cetuximab, Panitumumab)	Inhibition of distal tubule magnesium uptake causing hypomagnesemia-induced hypokalemia
Ifosfamide	Proximal tubule injury and partial Fanconi syndrome
Cisplatin	Hypomagnesemia-induced hypokalemia
Light chains	Proximal tubule injury and partial Fanconi syndrome

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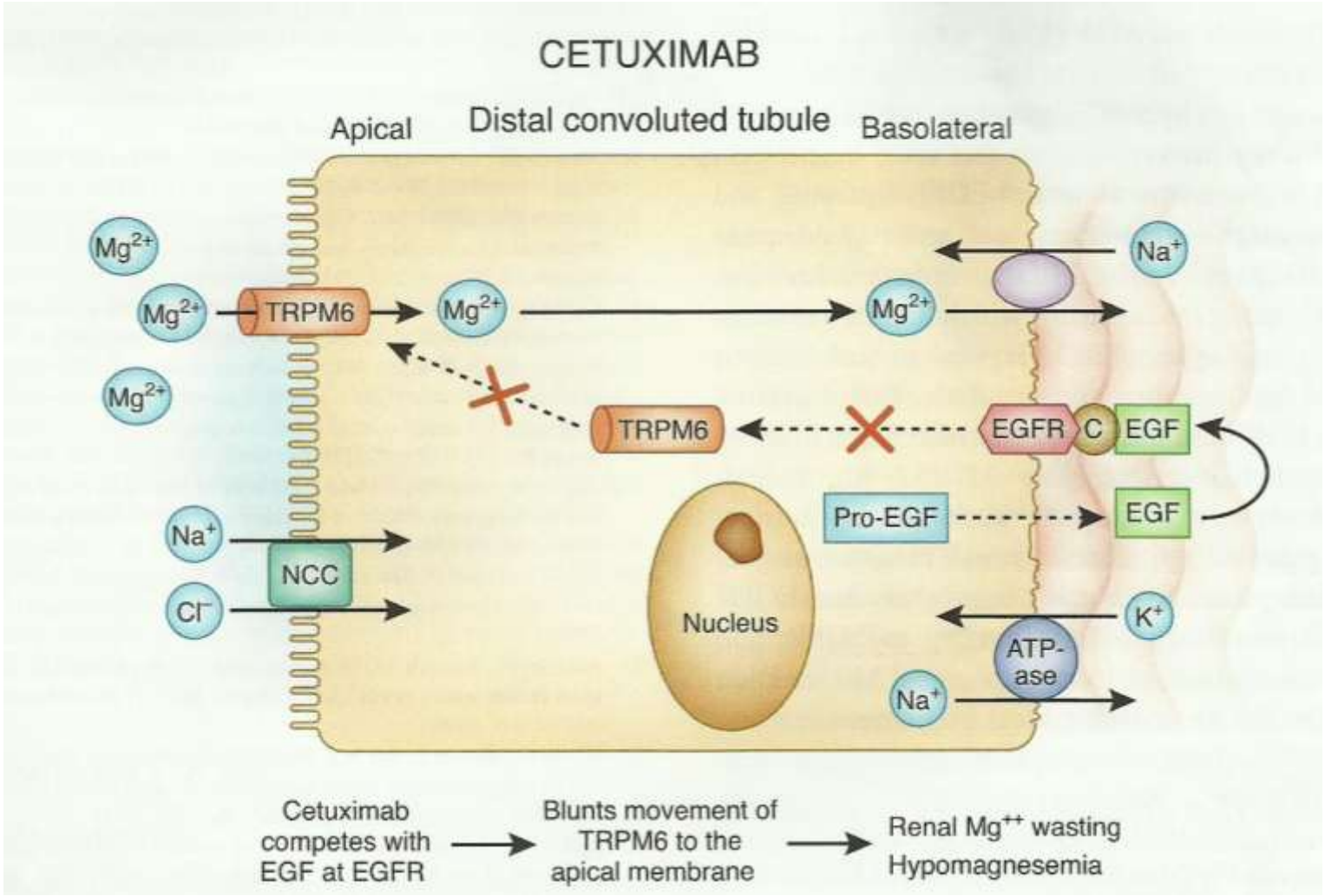
4. Hypomagnesemia



Clin J Am Soc Nephrol 7: 1713-1721, 2012.

TO DIALYSE OR NOT ???????

Attending Rounds

To Dialyze or Not: The Patient with Metastatic Cancer and AKI in the Intensive Care Unit

Alvin H. Moss

Clin J Am Soc Nephrol 7: 1507–1512, 2012. doi: 10.2215/CJN.02030212

- A 58-year-old woman with morbid obesity (body mass index . 90 kg/m2) was admitted to the hospital with back pain and iron deficiency anemia due to postmenopausal bleeding.
- Serum creatinine 0.4 mg/dl. Urinalysis shows 30 mg/dl of protein.
- Imaging studies revealed multiple mediastinal masses and large lymph nodes.
- A lymph node biopsy revealed metastatic squamous cell cancer of unknown primary.
- Her course was further complicated by multiple drug-resistant infections, septic shock, respiratory failure necessitating mechanical ventilation and tracheostomy, and anuric AKI.

- 4weeks into her hospitalization, the nephrology service was consulted for evaluation and management of AKI, which was thought to be due to acute tubular necrosis from septic shock.
- The patient was poorly responsive and could not respond to questions or commands.
- After 7 days of anuria, her BUN peaked at 86 mg/dl and her serum creatinine peaked at 3.6 mg/dl.
- The patient was on high ventilator settings (FIO2 50%; PEEP10 cm H2O; and pressure control, 22 cm H2O). She was unable to be weaned from mechanical ventilation, with PCO2 levels of approximately 70 mmHg.
- She was 30 L positive for the admission and had anasarca.
- Potential indications for dialysis included uremia and fluid overload with compromised oxygenation.

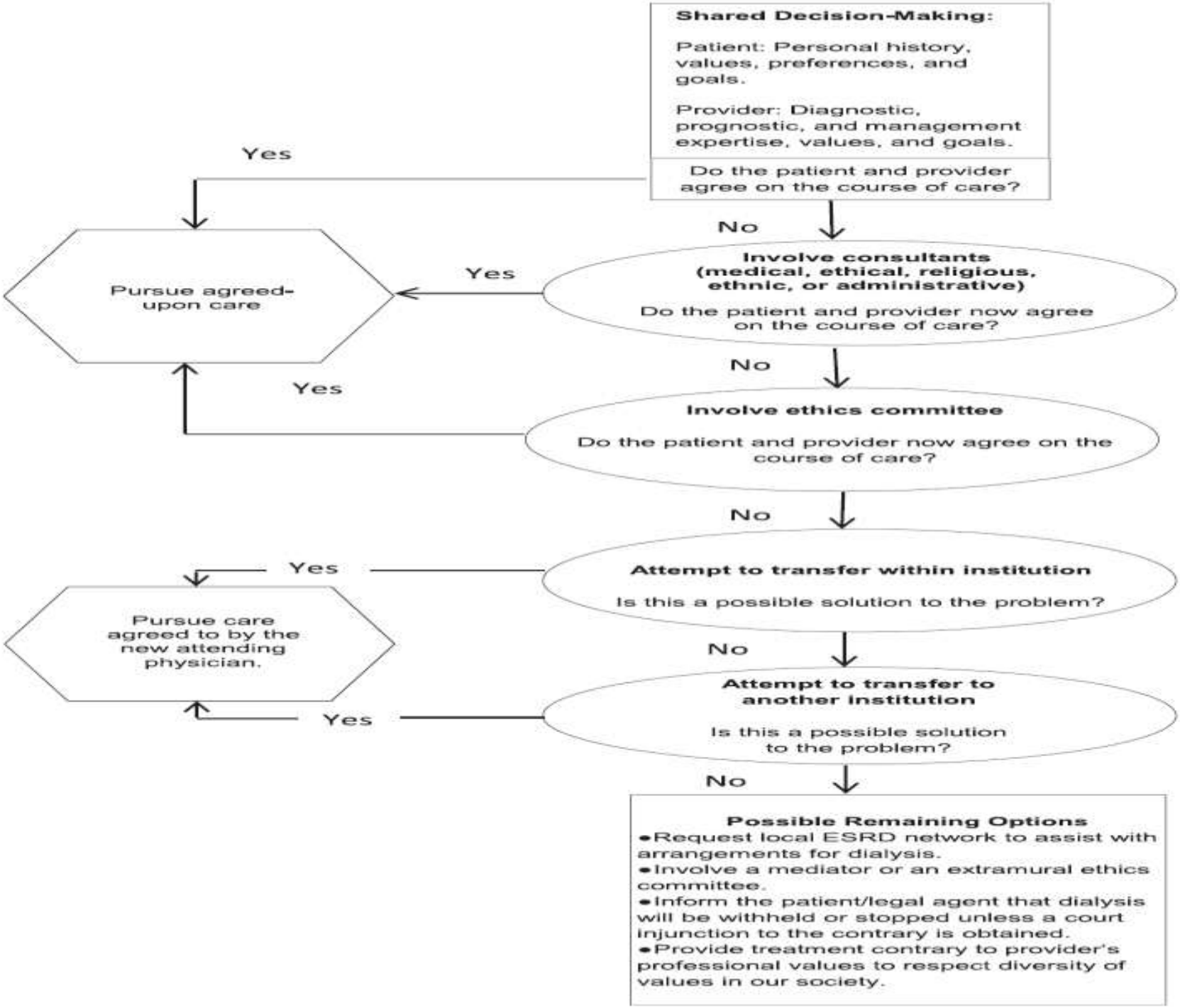
TO DIALYSE OR NOT ???????

Table 1. The seven-step process of ethical decision-making in patient care

Step 1. What are the ethical questions?
Step 2. What are the clinically relevant facts?
Step 3. What are the values at stake for all relevant parties?
Step 4. List options. What could you do?
Step 5. What should you do? Choose the best option from the ethical point of view.
Step 6. Justify your choice. Give reasons to support your choice. Refer back to the values and explain why some values are more important in this case than the others.
Step 7. How could this ethical issue have been prevented? Would any policies/guidelines/practices be useful in changing any problems with the system?

Table 2. Deciding what to offer: the four topics to be considered in ethical analysis

Medical indications
Patient preferences
Quality of life
Contextual features


Shared Decision-Making:
Patient: Personal history, values, preferences, and goals.
Provider: Diagnostic, prognostic, and management expertise, values, and goals.
Do the patient and provider agree on the course of care?
Yes
No
Involve consultants (medical, ethical, religious, ethnic, or administrative)
Do the patient and provider now agree on the course of care?
Yes
Pursue agreed-upon care
No
Involve ethics committee
Do the patient and provider now agree on the course of care?
Yes
No
Attempt to transfer within institution
Is this a possible solution to the problem?
Yes
Pursue care agreed to by the new attending physician.
No
Attempt to transfer to another institution
Is this a possible solution to the problem?
Yes
No
Possible Remaining Options
•Request local ESRD network to assist with arrangements for dialysis.
•Involve a mediator or an extramural ethics committee.
•Inform the patient/legal agent that dialysis will be withheld or stopped unless a court injunction to the contrary is obtained.
•Provide treatment contrary to provider's professional values to respect diversity of values in our society.

Conclusion

- Onco-Nephrology is a new and an emerging nephrology subspeciality.
- Increasing prevalence of cancers, development of new targeted therapies and increased age trend accepted for treatment created many complex renal proplems in cancer patients.
- Collaborative work between oncologists, nephrologists and intensivists is mandatory to improve care for cancer patients.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